

Authors	Author Address	Title	Publication	Abstract
Abu-Judeh HH, Levine S, Kumar M, el-Zeftawy H, Naddaf S, Lou JQ, Abdel-Dayem HM.	Department of Radiology, St. Vincent's Hospital, New York, NY 10011, USA.	Comparison of SPET brain perfusion and 18F-FDG brain metabolism in patients with chronic fatigue syndrome.	Nucl Med Commun 1998 Nov;19(11):1065-71	Chronic fatigue syndrome is a clinically defined condition of uncertain aetiology. We compared 99Tcm-HMPAO single photon emission tomography (SPET) brain perfusion with dual-head 18F-FDG brain metabolism in patients with chronic fatigue syndrome. Eighteen patients (14 females, 4 males), who fulfilled the diagnostic criteria of the Centers for Disease Control for chronic fatigue syndrome, were investigated. Thirteen patients had abnormal SPET brain perfusion scans and five had normal scans. Fifteen patients had normal glucose brain metabolism scans and three had abnormal scans. We conclude that, in chronic fatigue syndrome patients, there is discordance between SPET brain perfusion and 18F-FDG brain uptake. It is possible to have brain perfusion abnormalities without corresponding changes in glucose uptake.
Ambrogetti A, Leslie G. Olson, David C. Sutherland, John A. Malcolm, David Bliss, Stephen G. Gyulay		Daytime Sleepiness and REM Sleep Abnormalities in Chronic Fatigue A Case Series	Journal of Chronic Fatigue Syndrome 1998; 4(1): 23 - 35	Objective: To describe a subgroup of patients with chronic fatigue in whom there is increased physiological sleep tendency. Design: Prospective case series. Setting and Patients: Fifty-six consecutive patients with a working diagnosis of chronic fatigue syndrome underwent a sleep interview, overnight polysomnography and a Multiple Sleep Latency Test in a regional Sleep Disorders Center. Results: Of the 56 patients, 14 satisfied the current International Classification of Sleep Disorders criteria for the diagnosis of narcolepsy. Four of these patients had both excessive somnolence and clear-cut cataplexy and 10 pathological somnolence and polysomnographic criteria for narcolepsy. A further 35 had either increased daytime sleepiness, abnormal REM sleep regulation or both. Despite the objective evidence of daytime increased sleep tendency, the majority of the patients complained of fatigue and not of sleepiness. Twenty-nine patients were treated with either dexamphetamine or methylphenidate with good results in about half. Conclusion: We conclude that among patients investigated for chronic fatigue syndrome it is possible to identify a subgroup with significant daytime sleepiness and REM sleep abnormalities. Symptomatic treatment of these patients is often rewarding.
Andersson M, Bagby JR, Dyrehag L, Gottfries C.	Pain Unit, Kungälv Hospital, Sweden	Effects of staphylococcus toxoid vaccine on pain and fatigue in patients with fibromyalgia/chronic fatigue syndrome.	Eur J Pain 1998;2(2):133-142	Positive results of pilot studies of the effect of staphylococcus toxoid vaccine in patients with fibromyalgia and chronic fatigue syndrome were the incitement to the present, placebo-controlled study. It included 28 patients who fulfilled the criteria for both fibromyalgia and chronic fatigue syndrome. The effect of vaccination with a staphylococcus toxoid was compared with the effect of injections of sterile water. Psychometric assessment was made using 15 items from the comprehensive psychopathological rating scale (CPRS), Zung's self-rating depression scale and clinical global impressions (CGI). The visual analogue scale (VAS) was used to measure pain levels, and a hand-held electronic pressure algometer was used to measure pressure pain thresholds. Significant improvement was seen in seven of the 15 CPRS items in the vaccine group when pretreatment values were compared to post-treatment values. In CPRS <<fatiguability>>, there were significant intergroup differences, and in CPRS <<pain>> intergroup differences bordered on significance. There was no significant improvement in CPRS items in the placebo group. Clinical global impressions showed significant improvement in the vaccine-treated group, and VAS did so in both groups. In a follow-up study of 23 patients, the vaccine treatment was continued for 2-6 years. Fifty percent were rehabilitated successfully and resumed half-time or full-time work. The results of this study support the authors' hypothesis that treatment with staphylococcus toxoid may be a fruitful strategy in patients with fibromyalgia and chronic fatigue syndrome. Copyright 1998 European Federation of Chapters of the International Association for the Study of Pain.
Arzomand ML		Chronic Fatigue Syndrome Among School Children and Their Special Educational Needs	Journal of Chronic Fatigue Syndrome 1998; 4(3): 59 - 69	Objectives: To determine the prevalence of Chronic Fatigue Syndrome (CFS) in school children. To explore their Special Educational Needs (SEN) arrangements. To evaluate the views of their parents, the educational and medical professionals involved in the process of special education needs assessment. Design: A postal questionnaire survey. Setting: The Merton and Sutton Junior and High Schools. Subjects: Pupils diagnosed with CFS. Main Outcome Measures: Responses to CFS about special educational needs and case details. Results: With a 53.8% return rate, 22 cases were identified giving an overall point prevalence of 0.07%. Of these 22 cases, 21 were in Sutton and one in Merton. There were equal numbers of boys and girls. Although the respondent groups generally agreed about Special Educational Needs arrangements, differences existed on home tuition and physical education (PE) at school. Parents were more against PE, 5 (71%) vs. 2 (14%) and 4 (11%) of doctors and educational staff, respectively (P = 0.001). Four out of seven parents (57%) said home tuition was necessary, while only one doctor (7%) and nine educational staffs (25.7%) agreed with this (P = 0.044). Conclusion: The estimated overall prevalence is

				consistent with previous paediatric studies. Two different findings, however, emerged. The equal prevalence in boys and girls (in contrast to previous studies) and the highly significant difference of case numbers between these two neighbouring boroughs (21 vs. 1). Further research is needed for possible explanation of these differences.
Ayres JG, Flint N, Smith EG, Tunnicliffe WS, Fletcher TJ, Hammond K, Ward D, Marmion BP.	Department of Respiratory Medicine, Heartlands Hospital, Birmingham, UK.	Post-infection fatigue syndrome following Q fever.	QJM 1998 Feb;91(2):105-23	In 1989, 147 individuals in the West Midlands, UK, were infected with Q fever. Five years later, following anecdotal reports of fatigue, we used a questionnaire-based case-control study to determine the prevalence of chronic fatigue syndrome symptoms in this group. Replies from 71 patients were compared with those from 142 age- and sex-matched controls. Increased sweating (52.9% vs. 31.6%, $p = 0.006$), breathlessness (50.7% vs. 30.6%, $p = 0.006$), blurred vision (34.3% vs. 17.8%, $p = 0.016$) and undue tiredness (68.7% vs. 51.5%, $p = 0.03$) were found in controls compared to cases. These findings were similar to those in Australian abattoir workers occupationally exposed to Q fever. CDC criteria for chronic fatigue syndrome were fulfilled by 42.3% of cases and 26% of controls. Using visual analogue scores, symptoms were more severe in cases than in controls. Our findings support the existence of a chronic fatigue state following acute Q fever, in a group of patients exposed just once to the organism, and in circumstances free of such confounding factors as lawsuits over compensation.
Baraniuk JN, Clauw D, Yuta A, Ali M, Gaumont E, Upadhyayula N, Fujita K, Shimizu T.	Division of Rheumatology and Immunology and Allergy, Georgetown University, Washington, D.C. 20007-2197, USA.	Nasal secretion analysis in allergic rhinitis, cystic fibrosis, and nonallergic fibromyalgia/chronic fatigue syndrome subjects.	Am J Rhinol 1998 Nov-Dec;12(6):435-40	Rhinitis symptoms are present in approximately 70% of subjects with fibromyalgia and chronic fatigue syndrome (FM/CFS). Because only 35% to 50% have positive allergy skin tests, nonallergic mechanisms may also play a role. To better understand the mechanisms of nonallergic rhinitis in FM/CFS, nasal lavages were performed, and markers of vascular permeability, glandular secretion, and neutrophil and eosinophil infiltration measured in 27 nonallergic FM/CFS, 7 allergic rhinitis, 7 cystic fibrosis, and 9 normal subjects. Allergic rhinitis subjects had significantly increased vascular permeability (IgG) and ECP levels. Cystic fibrosis subjects had significantly higher elastase and total protein levels. There were no significant differences between FM/CFS and normal lavage fluids. Analysis of the constituents of nasal mucus provides information about ongoing secretory processes in rhinitis. There were no differences in the basal secretion of these markers of vascular permeability, submucosal gland serous cell secretion, eosinophil and neutrophil degranulation in nonallergic FM/CFS subjects. This suggests that constitutively active secretory processes that regulate continuous production of nasal secretions are not altered in FM/CFS. Future studies should examine alternative mechanisms such as inducible, irritant-activated, or reflex-mediated effects.
Baraniuk JN, Clauw DJ, Gaumont E.	Division of Rheumatology, Immunology and Allergy, Georgetown University, Washington, DC 20007-2197, USA.	Rhinitis symptoms in chronic fatigue syndrome.	Ann Allergy Asthma Immunol 1998 Oct;81(4):359-65	BACKGROUND: Atopy and allergic rhinitis are thought to be increased in prevalence in chronic fatigue syndrome (CFS). METHODS: To investigate this hypothesis, 51 CFS (CFS), 34 normal (N), 27 allergic rhinitis (AR), and 17 patients with other rheumatologic diseases filled out an Airway Symptom Severity self-report questionnaire to determine the frequencies of nasal, sinus, and chest symptoms, and a Systemic Complaints self-report questionnaire to determine the frequencies of complaints referable to neurologic, rheumatologic, gastrointestinal, and other systems. All subjects received a standard set of allergy skin tests, and were subdivided into those with positive and negative results. RESULTS: Allergy skin tests were positive in 35% of CFS and 44% of N subjects (difference not significant by Chi2). Significant rhinitis complaints were present in 83% of skin test positive CFS, 76% of skin test negative CFS, 74% of AR, and 23% of N subjects. Systemic Complaints scores were significantly elevated in skin test positive (94%) and negative (94%) CFS groups compared with AR (35%) and N (6%) groups. This score could significantly discriminate between CFS and N subjects. CONCLUSIONS: These data indicate that in this CFS population, 24% had no significant rhinitis complaints, 30% had positive skin tests suggesting the potential for allergic rhinitis complaints, and 46% had nonallergic rhinitis. The mechanism of the nonallergic component may offer insights into the pathogenesis of CFS.
Baraniuk JN, Daniel Clauw, Anna-Louisa MacDowell-Carneiro, Joseph Bellanti, Pavani Pandiri, Sukmun Foong, Mushtaq Ali		IgE Concentrations in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998; 4(1): 13 - 21	Hypothesis: Allergies have been proposed as a cause or contributing factor of chronic Fatigue syndrome (CFS). If this is so, then the stigmata of atopy, such as symptoms of allergic rhinitis and high serum IgE, should be present in CFS subjects. Methods: Medical records from an allergy and immunology clinic were retrospectively reviewed. All subjects who had had a serum IgE measurement performed over a 4-year period were identified, and allergy history and skin test data reviewed. Patients were then classified as: (a) allergic rhinitis ($n = 51$), (b) CFS ($n = 113$, 1992 criteria), and (c) normal subjects without atopy, CFS or immunodeficiency ($n = 76$). IgE levels were compared between groups. Results: A clinical history of allergic rhinitis was present in 31% (35/113) of the CFS subjects. The IgE levels of allergic rhinitis subjects and the subset of CPS subjects with allergic rhinitis were 392 ± 73 and 406 ± 123 IU/ml, respectively. In

				contrast, normal subjects and CFS subjects who did not give a history of allergic rhinitis had normal IgE levels of 49 ± 9 and 33 ± 4 IU/ml, respectively. Conclusion: Atopy with clinically defined allergic rhinitis, high IgE, positive allergy skin tests and the presumed TH2 lymphocyte-IgE-mast cell-eosinophil axis overactivity and immediate hypersensitivity (Type I) immune response was present in a minority of CFS subjects. While atopy may coexist in some CFS subjects, it is unlikely that atopy plays a causal role in CFS pathogenesis.
Baschetti R.		Chronic fatigue syndrome.	Postgrad Med J 1998 Nov;74(877):701 Comment on: Postgrad Med J. 1998 Apr;74(870):229-32	
Baschetti R.		Chronic fatigue syndrome.	JAMA 1998 Feb 11;279(6):431-2; discussion 432-3 Comment on: JAMA. 1997 Oct 8;278(14):1179-85	
Baschetti R.		Treatment for chronic fatigue syndrome.	Arch Intern Med 1998 Nov 9;158(20):2266-7 Comment on: Arch Intern Med. 1998 Apr 27;158(8):908-14	
Behan WMH, Ian J. Holt, David H. Kay, Pamela Moonie		In vitro Study of Muscle Aerobic Metabolism in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 5(1): 3 - 16	The purpose of this study was to establish if muscle aerobic metabolism is abnormal in chronic fatigue syndrome (CFS). Myoblast cultures from muscle biopsies of 16 patients with CFS and 10 healthy controls were established. Micromethods were used to determine the lactate/pyruvate (L/P) ratio, respiratory chain function and cytochrome oxidase and lactic dehydrogenase activities. Mitochondrial DNA (mtDNA) volume was measured and mtDNA rearrangements sought. The results showed that myoblasts from ten of 16 cases of CFS had defects in aerobic metabolism: two had increased L/P ratios, suggestive of a defect in oxidative phosphorylation while eight had decreased ratios, consistent with a deficiency in pyruvate dehydrogenase. There was a statistically significant broader range of L/P ratios in the patients' cultures, compared to controls ($p = 0.011$). No mtDNA rearrangements were present. This in vitro study confirms that there is convincing evidence of mild aerobic defects in skeletal muscle in some cases of CFS
Bell IR, Baldwin CM, Russek LG, Schwartz GE, Hardin EE.	Department of Psychiatry, University of Arizona, Tucson, USA.	Early life stress, negative paternal relationships, and chemical intolerance in middle-aged women: support for a neural sensitization model.	J Womens Health 1998 Nov;7(9):1135-47	This study (ntotal = 35) compared early life stress ratings, parental relationships, and health status, notably orthostatic blood pressures, of middle-aged women with low-level chemical intolerance (CI group) and depression, depressives without CI (DEP group), and normals. Environmental chemical intolerance is a symptom of several controversial conditions in which women are overrepresented, that is, sick building syndrome, multiple chemical sensitivity, chronic fatigue syndrome, and fibromyalgia. Previous investigators have postulated that people with CI have variants of somatization disorder, depression, posttraumatic stress disorder (PTSD) initiated by childhood abuse or a toxic exposure event. One neurobehavioral model for CI, somatization disorder, recurrent depression, and PTSD is neural sensitization, that is, the progressive amplification of host responses (e.g., behavioral, neurochemical) to repeated intermittent stimuli (e.g., drugs, chemicals, endogenous mediators, stressors). Females are more vulnerable to sensitization than are males. Limbic and mesolimbic pathways mediate central nervous system sensitization. Although both CI and DEP groups had high levels of life stress and past abuse, the CI group had the most distant and weak paternal relationships and highest limbic somatic dysfunction subscale scores. Only the CI group showed sensitization of sitting blood pressures over sessions. Together with prior evidence, these data are consistent with a neural sensitization model for CI in certain women. The findings may have implications for poorer long-term medical as well as neuropsychiatric health outcomes of a subset of women with CI. Subsequent research should test this model in specific clinical diagnostic groups with CI.
Bell IR, Baldwin CM, Schwartz GE.	Department of Psychiatry, University of Arizona, Tucson Veterans Affairs Medical Center, 85723, USA.	Illness from low levels of environmental chemicals: relevance to chronic fatigue syndrome and fibromyalgia.	Am J Med 1998 Sep 28;105(3A):74S-82S	This article summarizes (1) epidemiologic and clinical data on the symptoms of maladies in association with low-level chemicals in the environment, i.e., environmental chemical intolerance (CI), as it may relate to chronic fatigue syndrome (CFS) and fibromyalgia; and (2) the olfactory-limbic neural sensitization model for CI, a neurobehavioral synthesis of basic and clinical research. Severe CI is a characteristic of 20-47% of individuals with apparent CFS and/or fibromyalgia, all patients with multiple chemical sensitivity (MCS), and approximately 4-6% of the general population. In the general population, 15-30% report at

				<p>least minor problems with CI. The levels of chemicals reported to trigger CI would normally be considered nontoxic or subtoxic. However, host factors--e.g., individual differences in susceptibility to neurohormonal sensitization (amplification) of endogenous responses--may contribute to generating a disabling intensity to the resultant multisystem dysfunctions in CI. One site for this amplification may be the limbic system of the brain, which receives input from the olfactory pathways and sends efferents to the hypothalamus and the mesolimbic dopaminergic [reward] pathway. Chemical, biologic, and psychological stimuli can initiate and elicit sensitization. In turn, subsequent activation of the sensitized limbic and mesolimbic pathways can then facilitate dysregulation of behavioral, autonomic, endocrine, and immune system functions. Research to date has demonstrated the initiation of neurobehavioral sensitization by volatile organic compounds and pesticides in animals, as well as sensitizability of cardiovascular parameters, beta-endorphin levels, resting EEG alpha-wave activity, and divided-attention task performance in persons with CI. The ability of multiple types of widely divergent stimuli to initiate and elicit sensitization offers a new perspective on the search for mechanisms of illness in CFS and fibromyalgia with CI.</p>
<p>Bell IR, Patarca R, Baldwin CM, Klimas NG, Schwartz GE, Hardin EE.</p>	<p>Department of Psychiatry, Psychology, Family and Community Medicine, University of Arizona Health Sciences Center, and the Department of Psychiatry, Tucson Veterans Affairs Medical Center, Tucson, Ariz., USA.</p>	<p>Serum neopterin and somatization in women with chemical intolerance, depressives, and normals.</p>	<p>Neuropsychobiology 1998;38(1):13-8</p>	<p>The symptom of intolerance to low levels of environmental chemicals (CI, chemical intolerance) is a feature of several controversial polysymptomatic conditions that overlap symptomatically with depression and somatization, i.e., chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity, and Persian Gulf syndrome. These syndromes can involve many somatic symptoms consistent with possible inflammation. Immunological or neurogenic triggering might account for such inflammation. Serum neopterin, which has an inverse relationship with l-tryptophan availability, may offer a marker of inflammation and macrophage/monocyte activation. This study compared middle-aged women with CI (who had high levels of affective distress; n = 14), depressives without CI (n = 10), and normals (n = 11). Groups did not differ in 4 p.m. resting levels of serum neopterin. However, the CI alone had strong positive correlations between neopterin and all of the scales measuring somatization. These preliminary findings suggest the need for additional research on biological correlates of 'unexplained' multiple somatic symptoms in subtypes of apparent somatizing disorders.</p>
<p>Bennett R.</p>	<p>Department of Medicine, Oregon Health Sciences Center, Portland 97201, USA.</p>	<p>Fibromyalgia, chronic fatigue syndrome, and myofascial pain.</p>	<p>Curr Opin Rheumatol 1998 Mar;10(2):95-103</p>	<p>Epidemiologic studies continue to provide evidence that fibromyalgia is part of a spectrum of chronic widespread pain. The prevalence of chronic widespread pain is several times higher than fibromyalgia as defined by the 1990 American College of Rheumatology guidelines. There is now compelling evidence of a familial clustering of fibromyalgia cases in female sufferers; whether this clustering results from nature or nurture remains to be elucidated. A wide spectrum of fibromyalgia-associated symptomatology and syndromes continues to be described. During the past year the association with interstitial cystitis has been explored, and neurally mediated hypotension has been documented in both fibromyalgia and chronic fatigue syndrome. Abnormalities of the growth hormone-insulin-like growth factor-1 axis have been also documented in both fibromyalgia and chronic fatigue syndrome. The commonly reported but anecdotal association of fibromyalgia with whiplash-type neck trauma was validated in a report from Israel. However, unlike North America, 100% of Israeli patients with posttraumatic fibromyalgia returned to work. Basic research in fibromyalgia continues to pinpoint abnormal sensory processing as being integral to understanding fibromyalgia pain. Drugs such as ketamine, which block N-methyl-D-aspartate receptors (which are often upregulated in central pain states) were shown to benefit fibromyalgia pain in an experimental setting. The combination of fluoxetine and amitriptyline was reported to be more beneficial than either drug alone in patients with fibromyalgia. A high prevalence of autoantibodies to cytoskeletal and nuclear envelope proteins was found in chronic fatigue syndrome, and an increased prevalence of antipolymer antibodies was found in symptomatic silicone breast implant recipients who often have fibromyalgia.</p>
<p>Berwaerts J, Greta Moorkens, Roger Abs</p>		<p>Review of Neuroendocrine Disturbances in the Chronic Fatigue Syndrome Indications for a Role of the Growth Hormone-IGF-1 Axis in the Pathogenesis</p>	<p>Journal of Chronic Fatigue Syndrome 1998; 4(4): 81 - 91</p>	<p>The investigation of the growth hormone (GH)-IGF-1 axis in patients with chronic fatigue syndrome (CFS) may be important for different reasons. Some of the disturbances of the hypothalamic-pituitary-adrenal axis and central serotonergic (5-HT) function in CFS will be reviewed, before elaborating on three hypotheses that may explain the role of a disturbed GH axis activity in CFS. Firstly, the disturbed central 5-HT receptor activity may be the cause of GH axis dysfunction. Secondly, CFS may be considered as a "stress-related illness," in which the disturbed central 5-HT function is a result rather than the cause of impaired neuroendocrine stress responses. Finally, by analogy with fibromyalgia, sleep abnormalities in CFS may impair nocturnal GH secretion. Whether the disturbed GH axis activity is a primary or secondary</p>

<p>Berwaerts J, Moorkens G, Abs R.</p>	<p>Department of Endocrinology, Middelheim Hospital, Antwerp, Belgium.</p>	<p>Secretion of growth hormone in patients with chronic fatigue syndrome.</p>	<p>Growth Horm IGF Res 1998 Apr;8 Suppl B:127-9</p>	<p>phenomenon in the pathogenesis of CFS, should be elucidated by future clinical investigations.</p> <p>Decreased serum levels of insulin-like growth factor I (IGF-I) are common in patients with fibromyalgia, which is frequently associated with chronic fatigue syndrome (CFS). Twenty patients with CFS (7 men, 13 women; age range, 30-60 years) and age- and sex-matched controls were tested for peak GH responses to insulin-induced hypoglycaemia and arginine administration. Nocturnal secretion of GH and serum levels of IGF-I were also measured. Serum IGF-I SDS (SD) was significantly lower in patients with CFS than in controls (SDS, -0.39 1.07 vs 0.33 0.84; P = 0.02). Patients with CFS also tended to have reduced nocturnal secretion of GH (area under the curve, 32.4 18.3 vs 62.7 43.7 microg/l/15 minutes; P= 0.06), but peak GH responses to insulin-induced hypoglycaemia and arginine administration did not differ significantly between the two groups. It is not clear whether the tendency for impaired spontaneous nocturnal GH secretion in patients with CFS is a cause or an effect of the condition.</p>
<p>Blackwood SK, MacHale SM, Power MJ, Goodwin GM, Lawrie SM.</p>	<p>Edinburgh University Department of Psychiatry, Royal Edinburgh Hospital, UK.</p>	<p>Effects of exercise on cognitive and motor function in chronic fatigue syndrome and depression.</p>	<p>J Neurol Neurosurg Psychiatry 1998 Oct;65(4):541-6</p>	<p>OBJECTIVES: Patients with chronic fatigue syndrome complain of physical and mental fatigue that is worsened by exertion. It was predicted that the cognitive and motor responses to vigorous exercise in patients with chronic fatigue syndrome would differ from those in depressed and healthy controls. METHODS: Ten patients with chronic fatigue syndrome, 10 with depressive illness, and 10 healthy controls completed cognitive and muscle strength testing before and after a treadmill exercise test. Measures of cardiovascular functioning and perceived effort, fatigue, and mood were taken during each stage of testing. RESULTS: Depressed patients performed worst on cognitive tests at baseline. During the treadmill test, patients with chronic fatigue syndrome had higher ratings of perceived effort and fatigue than both control groups, whereas patients with depression reported lower mood. After exertion, patients with chronic fatigue syndrome showed a greater decrease than healthy controls on everyday tests of focused (p=0.02) and sustained (p=0.001) attention, as well as greater deterioration than depressed patients on the focused attention task (p=0.03). No between group differences were found in cardiovascular or symptom measures taken during the cognitive testing. CONCLUSIONS: Patients with chronic fatigue syndrome show a specific sensitivity to the effects of exertion on effortful cognitive functioning. This occurs despite subjective and objective evidence of effort allocation in chronic fatigue syndrome, suggesting that patients have reduced working memory capacity, or a greater demand to monitor cognitive processes, or both. Further insight into the pathophysiology of the core complaints in chronic fatigue syndrome is likely to be realised by studying the effects of exercise on other aspects of everyday functioning.</p>
<p>Block W, Traber F, Kuhl CK, Keller E, Lamerichs R, Karitzky J, Rink H, Schild HH.</p>	<p>Radiologische Klinik der Universitat Bonn. block@uni-bonn.de</p>	<p>[31P-mr spectroscopy of peripheral skeletal musculature under load: demonstration of normal energy metabolites compared with metabolic muscle diseases].[article in German]</p>	<p>Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr 1998 Mar;168(3):250-7</p>	<p>PURPOSE: 31P-MR spectroscopy of skeletal muscle under exercise was used to obtain the range of normal variation and comparison was made for different neuromuscular diseases. METHODS: 41 examinations of 24 volunteers and 41 investigations in 35 patients were performed on 1.5 T MR systems (Gyrosan 515 und S15/ACSII, Philips). Localised 31P-MR spectra of the calf muscle were obtained in time series with a resolution of 12 s. RESULTS: Two types of muscle energy metabolism were identified from the pattern of spectroscopic time course in volunteers: While the first group was characterised by a remarkable decline to lower pH values during exercise, the second group showed only small pH shifts (minimum pH: 6.48 0.13 vs 6.87 0.07, p < 10(-6)) although comparable workload conditions were maintained. The pH-values correlated well with blood lactate analysis. Patients with metabolic disorders and chronic fatigue syndrome (CFS) showed decreased resting values of PCr/(PCr Pi) and increased pH levels during exercise. PCr recovery was significantly delayed (0.31 vs 0.65 min-1, p < 0.00005) in metabolic muscle disorders but was normal in CFS patients. CONCLUSION: Findings in volunteers indicate utilisation of different metabolic pathways which seems to be related to the fibre type composition of muscle. Reduced resting levels for PCr/(PCr Pi), altered pH time courses, and decreased PCr recovery seem to be helpful indicators for diagnosis of metabolic muscle disorders.</p>
<p>Borish L, Schmaling K, DiClementi JD, Streib J, Negri J, Jones JF.</p>	<p>Department of Medicine, National Jewish Medical and Research Center, University of Colorado Health Sciences Center, Denver 80206, USA.</p>	<p>Chronic fatigue syndrome: identification of distinct subgroups on the basis of allergy and psychologic variables.</p>	<p>J Allergy Clin Immunol 1998 Aug;102(2):222-30</p>	<p>BACKGROUND: We investigated a role for allergic inflammation and psychologic parameters in the development of chronic fatigue syndrome (CFS). METHODS: The design was a comparison between subjects with CFS and age- and sex-matched control cohorts. Studies were performed on CFS subjects (n = 18) and control cohorts consisting of normal subjects (n = 11), allergic subjects (n = 14), and individuals with primary depression (n = 12). We quantified cytokines at baseline as cell-associated immunoreactive peptides and as transcripts evaluated by means of semiquantitative RNA-based polymerase chain reactions. Psychologic evaluations included administration of the Diagnostic Interview Schedule, the Structured Clinical Interview, and the Symptom Checklist 90-Revised. RESULTS: Increases in tumor necrosis factor</p>

				<p>(TNF)-alpha were identified in individual subjects with CFS (50.1 14.4 pg TNF-alpha per 10(7) peripheral blood mononuclear cells [PBMCs]; mean SEM) and allergic subjects (41.6 7.6) in comparison with normal subjects (13.1 8.8) (P < .01 and P < .05, respectively). Similar trends were observed for interferon (IFN)-alpha in allergic subjects (3.0 1.7 pg/10(7) PBMCs) and subjects with CFS (6.4 3.4) compared with normal subjects (1.9 1.4). A significant increase (P < .05) in TNF-alpha transcripts was demonstrated between subjects with CFS and depressed subjects. In contrast to these proinflammatory cytokines, both subjects with CFS (2.6 1.8 pg/10(7) PBMCs) and allergic subjects (3.4 2.8) were associated with a statistically significant (P < .01) decrease in IL-10 concentrations compared with normal subjects (60.2 18.2). As shown in other studies, most of our subjects with CFS were allergic (15 of 18) and therefore presumably demonstrated cytokine gene activation on that basis. The seasonal exacerbation of allergy was associated with a further increase in cellular IFN-alpha (from 2.1 1.2 to 14.2 4.5 pg/107 PBMCs; P < .05) but no further modulation of TNF-alpha or IL-10. Similarly, self-reported exacerbations of CFS were associated with a further increase in IFN-alpha (from 2.5 1.0 to 21.9 7.8; P < .05) and occurred at times of seasonal exposures to allergens. This linkage does not permit making any definitive conclusions regarding a causative influence of either seasonal allergies or the increase in cellular IFN-alpha with the increase in CFS symptoms. The close association between atopy and CFS led us to speculate that CFS may arise from an abnormal psychologic response to the disordered expression of these proinflammatory and antiinflammatory cytokines. Psychologic variables were predictive of immune status within the CFS sample (65.9% of the variance in immune status; F (3,10) = 6.44, P < .05). Specifically, the absence of a personality disorder but greater endorsement of global psychiatric symptoms was predictive of immune activation. CONCLUSIONS: Most of our subjects with CFS were allergic, and the CFS and allergy cohorts were similar in terms of their immune status. However, the CFS subjects could be discriminated by the distinct psychologic profiles among subjects with and without immune activation. We propose that in at least a large subgroup of subjects with CFS who had allergies, the concomitant influences of immune activation brought on by allergic inflammation in an individual with the appropriate psychologic profile may interact to produce the symptoms of CFS. In a psychologically predisposed individual, symptoms associated with allergic inflammation are recognized as illness.</p>
Borok G		Chronic Fatigue Syndrome An Atopic State	Journal of Chronic Fatigue Syndrome 1998; 4(3): 39 - 57	<p>The cause of the tiredness and depression, may be due to a virus in the acute or recuperative phase, but in the long-term fatigue must be due to other mechanisms. As varied as are our size, shape, skin and eye colour so are the more subtle nuances of antibodies and enzymes which each cell produces. It is postulated that it is mostly atopic patients who will also react abnormally to certain foods, inhalants and skin applications. Sugars (refined foods) play a major role in leading to fatigue by their chemical, physiological, pharmacological and glycosylogical properties. Bread plays a major role in provoking the symptoms of depression in the chronic fatigue syndrome. What is suggested is that in a genetically predisposed group of people food intolerance causes symptoms akin to both the major and minor criteria of CFS.</p>
Brown SL, Langone JJ, Brinton LA.		Silicone breast implants and autoimmune disease.	J Am Med Womens Assoc 1998 Winter;53(1):21-4, 40	<p>In 1992, the Food and Drug Administration requested a voluntary moratorium on the scale and implantation of silicone-gel-filled breast implants because of growing concern over the lack of scientific and clinical data supporting their safety and effectiveness. Breast implants had been reported to cause serious local complications, and new questions about breast implants and increased risk for autoimmune disease, including the rare but sometimes fatal connective tissue disease scleroderma, were also raised. Since that time, clinical studies have focused on the adjuvant effect of silicone and of potential autoantibody production. Epidemiologic studies have ruled out a large increased risk for connective tissue disease overall in women with breast implants, but samples were too small to rule out an increase in rare connective tissue diseases. Nor were studies properly designed to address whether an atypical syndrome might develop in women with breast implants. Meta-analyses of these studies cannot remedy their underlying methodologic weaknesses. While the question of whether rare connective tissue disease is associated with breast implants may never be answered definitively, recent progress in identifying new syndromes such as fibromyalgia and chronic fatigue syndrome may provide an insight into methodology for evaluating the existence of a silicone-related syndrome in women with breast implants.</p>
Bruno RL, Creange SJ, Frick NM.	Kids' Fatigue Management Program and The Post-Polio Institute, Englewood Hospital	Parallels between post-polio fatigue and chronic fatigue syndrome: a common	Am J Med 1998 Sep 28;105(3A):66S-73S	<p>Fatigue is the most commonly reported and most debilitating of post-polio sequelae affecting the >1.8 million North American polio survivors. Post-polio fatigue is characterized by subjective reports of difficulty with attention, cognition, and maintaining wakefulness. These symptoms resemble those reported</p>

	and Medical Center, New Jersey 07631, USA.	pathophysiology?		in nearly 2 dozen outbreaks of post-viral fatigue syndromes (PVFS) that have recurred during this century and that are related clinically, historically, anatomically, or physiologically to poliovirus infections. This article reviews recent studies that relate the symptoms of post-polio fatigue and chronic fatigue syndrome (CFS) to clinically significant deficits on neuropsychologic tests of attention, histopathologic and neuroradiologic evidence of brain lesions, impaired activation of the hypothalamic-pituitary-adrenal axis, increased prolactin secretion, and electroencephalogram (EEG) slow-wave activity. A possible common pathophysiology for post-polio fatigue and CFS, based on the Brain Fatigue Generator Model of PVFS, and a possible pharmacotherapy for PVFS based on replacement of depleted brain dopamine, will be described.
Bruno RL, Susan Creange, Jerald R. Zirmerman Nancy M. Frick		Elevated Plasma Prolactin and EEG Slow Wave Power in Post-Polio Fatigue Implications for a Dopamine Deficiency Underlying Post-Viral Fatigue Syndromes	Journal of Chronic Fatigue Syndrome 1998; 4(2): 61 - 75	To test the hypothesis that plasma prolactin and electroencephalographic (EEG) slow wave activity are correlated with fatigue, 33 polio survivors without medical or psychologic comorbidities were studied. Subjects were administered the Post-Polio Fatigue Questionnaire (PFQ) and had resting measurement of both plasma prolactin and bilateral temporal-occipital power across the EEG frequency spectrum. Typical daily fatigue severity on the PFQ was significantly correlated with daily difficulty with attention, staying awake and motivation, but not with measures of acute polio severity or the number of limbs affected by late-onset Post-Polio Sequelae symptoms. Prolactin was significantly correlated with daily fatigue severity on the PFQ ($r = .39$; $p < .05$). EEG power was equal between the two hemispheres across all frequency bands. However, EEG slow wave power in the right hemisphere was significantly correlated with daily fatigue severity and prolactin level ($r = .37$; $p < .05$). Using multiple linear regression, age at acute polio, frequency of difficulty with attention on the PFQ, prolactin and right hemisphere slow wave power predicted 72% of the variance of the daily fatigue severity rating ($r = .85$; $p < .0001$). These data suggest that increased prolactin secretion and EEG slowing are related to the severity of post-polio fatigue, findings similar to those in patients with acute paralytic and non-paralytic poliomyelitis and with chronic fatigue syndrome. A primary role is suggested for a dopamine deficiency (versus serotonergic receptor supersensitivity) underlying impaired cortical activation and the symptoms associated with putative post-viral fatigue syndromes.
Calkins H, Rowe PC.	The Johns Hopkins University School of Medicine, Baltimore, Maryland.	Relationship Between Chronic Fatigue Syndrome and Neurally Mediated Hypotension.	Cardiol Rev 1998 May;6(3):125-134	Chronic fatigue syndrome is a chronic debilitating disease that afflicts 4/1000 of the general population. The pathophysiologic basis for this condition is unknown, and no known consistently effective therapy has been identified. Recent studies have reported a link between the chronic fatigue syndrome and neurally mediated hypotension, a common abnormality of blood pressure regulation. In nonrandomized studies, treatment directed at neurally mediated hypotension has been effective in treating the symptoms of the chronic fatigue syndrome in two-thirds of patients. Prospective randomized trials are now in progress.
Cannon JG, Angel JB, Abad LW, O'Grady J, Lundgren N, Fagioli L, Komaroff AL.	Department of Medicine, New England Medical Center, Boston, Massachusetts, USA. jgc2@psu.edu	Hormonal influences on stress-induced neutrophil mobilization in health and chronic fatigue syndrome.	J Clin Immunol 1998 Jul;18(4):291-8	This investigation tested the hypotheses that women diagnosed with chronic fatigue syndrome (CFS) would exhibit significantly greater systemic indices of exercise-induced leukocyte mobilization and inflammation (neutrophilia, lactoferrin release, complement activation) than controls matched for age, weight, and habitual activity and that responses in the luteal phase of the menstrual cycle would be greater than in the follicular phase. Subjects stepped up and down on a platform adjusted to the height of the patella for 15 min, paced by metronome. Blood samples were collected under basal conditions (the day before exercise) and following exercise for determination of circulating neutrophils and plasma concentrations of lactoferrin, C3a des arg, and creatine kinase. Complete, 24-hr urine collections were made for determination of cortisol excretion. For all subjects, circulating neutrophil counts increased 33% ($P < 0.0001$) and lactoferrin increased 27% ($P = 0.0006$) after exercise, whereas plasma C3a des arg and creatine kinase did not increase. No indication of an exaggerated or excessive response was observed in the CFS patients compared to the controls. In healthy women, circulating neutrophil numbers exhibited previously described relationships with physiological variables: basal neutrophil counts correlated with plasma progesterone concentrations ($R = 0.726$, $P = 0.003$) and the exercise-induced neutrophilia correlated with both urinary cortisol ($R = 0.660$, $P = 0.007$) and plasma creatine kinase ($R = 0.523$, $P = 0.038$) concentrations. These relationships were not observed in the CFS patients ($R = 0.240$, $P = 0.370$; $R = 0.042$, $P = 0.892$; and $R = 0.293$, $P = 0.270$; respectively). These results suggest that normal endocrine influences on the circulating neutrophil pool may be disrupted in patients with CFS.
Capen K.		Chronic fatigue syndrome get court's nod of approval as legitimate disorder.	CMAJ 1998 Sep 8;159(5):533-4Comment in: CMAJ. 1999 Mar	Lawyer Karen Capen looks at the implications of a recent Alberta court case involving chronic fatigue syndrome. She thinks Canada's physicians should pay close attention to this precedent-setting case.

			9;160(5):636, 638 CMAJ. 1999 Mar 9;160(5):638	
Caplan C.		Chronic fatigue syndrome or just plain tired?	CMAJ 1998 Sep 8;159(5):519-20 Comment in: CMAJ. 1999 Mar 9;160(5):636, 638 CMAJ. 1999 Mar 9;160(5):638	
Cathebras P, Lauwers A, Rousset H.	Service de Medecine Interne, Hopital Nord, Saint-Etienne.	[Fibromyalgia. A critical review].[article in French]	Ann Med Interne (Paris) 1998 Nov;149(7):406-14	Fibromyalgia is a chronic pain syndrome, more common in women. Its prevalence is estimated around 2% in the general population, and up to 20% among rheumatology outpatients. Besides musculoskeletal pain, symptoms as fatigue and sleep disturbance are considered characteristic. Research criteria have been set up, but their seemingly preciseness is unable to distinguish clearly between fibromyalgia and other functional somatic syndromes (chronic fatigue syndrome, irritable bowel syndrome) and psychiatric disorders (depression, anxiety), with which a striking comorbidity is documented. The diagnosis of fibromyalgia does not theoretically require the exclusion of muscle, joint, or metabolic diseases, but in clinical practice this problem proves to be of crucial importance. There are numbers of pathophysiological hypothesis for fibromyalgia, but none of them is fully satisfying: muscle is probably innocent; sleep disturbance, although sometimes considered a landmark of the syndrome, is unspecific; stress response studies show subtle anomaly; psychiatric disorders may represent factors of vulnerability and perpetuation rather than causes. We propose to include some of these etiological contributors in vicious circles leading to a "final common pathway" characterized by generalized hyperalgesia. Treatments of fibromyalgia, whether pharmacological (antidepressants) or psychological (cognitive-behavioral therapies) are of little efficacy, and the global prognosis of fibromyalgia is poor. However, the outcome might prove better outside the specialized clinics in which studies of chronic sufferers with severe abnormal illness behaviors are done. The social consequences of the popularization of the diagnosis of fibromyalgia should not be neglected.
Chester AC.		Chronic fatigue syndrome.	JAMA 1998 Feb 11;279(6):432; discussion 432-3 Comment on: JAMA. 1997 Oct 8;278(14):1179-85	
Choppa PC, Vojdani A, Tagle C, Andrin R, Magtoto L.	Immunosciences Lab Incorporated Beverly Hills, CA, USA.	Multiplex PCR for the detection of Mycoplasma fermentans, M. hominis and M. penetrans in cell cultures and blood samples of patients with chronic fatigue syndrome.	Mol Cell Probes 1998 Oct;12(5):301-8	A multiplex polymerase chain reaction (PCR) was initially developed to detect the presence of mycoplasma genus DNA sequences in cell cultures and to differentiate between three human pathogenic mycoplasma species simultaneously. The assay in turn, proved to be a useful tool for the detection of mycoplasma infection in human DNA samples. One set of oligonucleotide primers which are specific for a highly conserved region among all members of the genus mycoplasma along with three other primer sets which are specific for Mycoplasma fermentans, Mycoplasma hominis and Mycoplasma penetrans species were used in this assay. The sensitivity of detection was determined by infecting peripheral blood mononuclear cells (PBMC) of healthy individuals with known bacterial copy numbers from each species, extracting the DNA, and subjecting 1 microgram of DNA from each sample to 40 cycles of amplification. By using agarose gel electrophoresis the detection level was determined to be 7, 7, 9 and 15 mycoplasma cells per microgram of human genomic DNA for M. genus, M. fermentans, M. hominis and M. penetrans, respectively. The assay was applied to DNA extracted from the PBMCs of individuals suffering from chronic fatigue syndrome (CFS) (n=100) as determined by the Center for Disease Control (CDC) criteria, and compared to healthy individuals (n=100). The percentage of M. genus infection was found to be 52% in CFS patients and only 15% in healthy individuals. Mycoplasma fermentans, M. hominis and M. penetrans were detected in 32, 9 and 6% of the CFS patients while they were detected in 8, 3 and 2% of the healthy control subjects, respectively. This assay provides a rapid and cost efficient procedure to screen either cell cultures or clinical samples for the presence of three potentially pathogenic species of mycoplasma with a high level of sensitivity and specificity. Copyright 1998 Academic Press.
Christodoulou C, DeLuca J, Lange G, Johnson SK, Sisto SA, Korn L, Natelson BH.	University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, USA.	Relation between neuropsychological impairment and functional disability in patients with chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1998 Apr;64(4):431-4 Comment in: J Neurol Neurosurg Psychiatry. 1998	OBJECTIVES: To examine the relation between neuropsychological impairment and functional disability in patients with chronic fatigue syndrome, and determine whether the relation is independent of psychiatric factors. METHODS: The subjects were 53 patients with chronic fatigue syndrome and 32 healthy controls who did not exercise regularly. Subjects were administered a structured psychiatric interview and completed questionnaires focusing on depression and functional disability. They also completed a battery

			Apr;64(4):430	of standardised neuropsychological tasks focusing on the cognitive domains that patients with chronic fatigue syndrome experience as particularly difficult: memory (verbal and visual), and attention/concentration. A test score was defined as failing when it was > or =2 SD below the mean of the healthy controls after controlling for demographic factors. RESULTS: Those patients with chronic fatigue syndrome with higher numbers of failing neuropsychological test scores reported significantly more days of general inactivity in the past month than those with fewer failing scores. This result remained significant even after partialling out the contribution of the presence of a comorbid axis I psychiatric episode and the overall level of depressive symptomatology. Patients with failing verbal memory scores were particularly functionally disabled compared with those with passing scores. CONCLUSION: A relation was found between cognitive impairment and functional disability which could not be explained entirely on the basis of psychiatric factors.
Cohen SI.		Increased illness experience preceding chronic fatigue syndrome.	J R Coll Physicians Lond 1998 May-Jun;32(3):274 Comment in: J R Coll Physicians Lond. 1998 Jul-Aug;32(4):389 and 1998 Jan-Feb;32(1):44-8	
Conti F, Pittoni V, Sacerdote P, Priori R, Meroni PL, Valesini G.	Istituto di Clinica Medica I, Universita degli Studi di Roma La Sapienza, Rome, Italy.	Decreased immunoreactive beta-endorphin in mononuclear leucocytes from patients with chronic fatigue syndrome.	Clin Exp Rheumatol 1998 Nov-Dec;16(6):729-32	OBJECTIVE: To investigate beta-endorphin concentrations in the peripheral blood mononuclear cells (PBMC) of patients with chronic fatigue syndrome (CFS). METHODS: Sixteen patients with CFS were enrolled in this study. Ten healthy subjects were studied as controls. Beta-endorphin concentrations were measured in PBMC by radioimmunoassay performed with antibodies specific for the C-terminal portion of human beta-endorphin. RESULTS: Beta-endorphin concentrations in the PBMC of chronic fatigue patients were significantly lower ($p < 0.001$) than in healthy subjects (mean SD: 8.5 7.0 vs. 42.6 22.6). CONCLUSION: Patients with CFS were found to have low levels of PBMC beta-endorphin. This finding may reflect the condition of chronic immune activation in CFS that has been reported in previous investigations. Beta-endorphin concentrations in PBMC seem to mirror the central nervous system homeostasis of the opioid. Therefore, we would postulate that the fatigue and weakness typical of CFS could be related to low beta-endorphin concentrations at the central nervous system level.
Corrado G, Riezzo G, Rea P, Pacchiarotti C, Cavaliere M, Cardì E.		Normal gastric emptying time and myoelectrical activity in an adolescent with chronic fatigue syndrome.	Ital J Gastroenterol Hepatol 1998 Aug;30(4):444-5	
Crofford LJ.	Division of Rheumatology, University of Michigan, Ann Arbor 48109-0680, USA. crofford@umich.edu	The hypothalamic-pituitary-adrenal stress axis in fibromyalgia and chronic fatigue syndrome.	Z Rheumatol 1998;57 Suppl 2:67-71	HPA axis abnormalities in FM, CFS, and other stress-related disorders must be placed in a broad clinical context. We know that interventions providing symptomatic improvement in patients with FM and CFS can directly or indirectly affect the HPA axis. These interventions include exercise, tricyclic anti-depressants, and serotonin reuptake inhibitors. There is little direct information as to how the specific HPA axis perturbations seen in FM can be related to the major symptomatic manifestations of pain, fatigue, sleep disturbance, and psychological distress. Since many of these somatic and psychological symptoms are present in other syndromes that exhibit HPA axis disturbances, it seems reasonable to suggest that there may be some relationship between basal and dynamic function of the HPA axis and clinical manifestations of FM and CFS.
Csef H.	Med. Poliklinik der Univ. Wurzburg.	[The non-specific environmental syndromes MCS (Multiple Chemical Sensitivity), IEI (Idiopathic Environmental Intolerance) and SBS (Sick Building Syndrome)].[article in German]	Fortschr Med 1998 Nov 30;116(33):18-20, 22, 24	This review starts with a clinical description of the most common unspecific environmental diseases, such as Multiple Chemical Sensitivities (MCS), Idiopathic Environmental Intolerances (IEI) and Sick Building Syndrome (SBS). These syndromes are very controversial discussed between scientific medicine and "clinical ecology". In addition, they have fundamental similarities to Chronic Fatigue Syndrome (CFS) and Fibromyalgia. Finally the spectrum of therapeutic approaches is discussed.
Cuykx V, Van Houdenhove B, Neerincx E.		Childhood abuse, personality disorder and chronic fatigue syndrome.	Gen Hosp Psychiatry 1998 Nov;20(6):382-4 Comment on: Gen Hosp Psychiatry.	

<p>De Becker P, Dendale P, De Meirleir K, Campine I, Vandendorpe K, Hagers Y.</p>	<p>Department of Human Physiology, University Hospital, Free University, Brussels, Belgium.</p>	<p>Autonomic testing in patients with chronic fatigue syndrome.</p>	<p>1994 Sep;16(5):319-25 Am J Med 1998 Sep 28;105(3A):22S-26S</p>	<p>The purpose of this study was to determine whether chronic fatigue syndrome (CFS) patients show autonomic dysfunction at the cardiac level and if so, to discover whether these abnormalities explain the fatigability and/or other symptoms in CFS. The study population consisted of 21 CFS patients (Centers for Disease Control and Prevention [CDC] criteria, 1988) and 13 age- and sex-matched healthy controls. The autonomic testing consisted of: (1) postural challenge: registration of heart rate and blood pressure (BP) and heart rate variability in supine and in upright position (tilted to 70 degrees); (2) Valsalva maneuver; (3) handgrip test; (4) cold pressor test; and (5) heart rate response to deep breathing. Statistical analysis was performed using the Mann Whitney rank sum test; results of the test were considered significant at the 0.05 level. After tilting heart rate was significantly higher in CFS patients compared with healthy controls (mean CFS = 88.9 beats/min vs control = 77.9 beats/min; $P < 0.01$). Low frequency power after tilting was significantly higher in CFS patients compared with controls (mean CFS = 0.603 vs control = 0.428; $P = 0.02$). There was a trend toward an increased heart rate during the cold pressor test. Other parameters did not differ between the CFS and control populations. The observed changes point toward a sympathetic overactivity in CFS patients when they are exposed to stress. Parasympathetic abnormalities could not be observed. Therefore, our findings provide no real explanation for the fatigue and intolerance to physical exertion in these patients.</p>
<p>De Lorenzo F, Hargreaves J, Kakkar VV.</p>	<p>Beatrice Research Centre, London, UK.</p>	<p>Phosphate diabetes in patients with chronic fatigue syndrome.</p>	<p>Postgrad Med J 1998 Apr;74(870):229-32 Comment in: Postgrad Med J. 1998 Nov;74(877):701</p>	<p>Phosphate depletion is associated with neuromuscular dysfunction due to changes in mitochondrial respiration that result in a defect of intracellular oxidative metabolism. Phosphate diabetes causes phosphate depletion due to abnormal renal re-absorption of phosphate by the proximal renal tubule. Most of the symptoms presented by patients with phosphate diabetes such as myalgia, fatigue and mild depression, are also common in patients with chronic fatigue syndrome, but this differential diagnosis has not been considered. We investigated the possible association between chronic fatigue syndrome and phosphate diabetes in 87 patients who fulfilled the criteria for chronic fatigue syndrome. Control subjects were 37 volunteers, who explicitly denied fatigue and chronic illness on a screening questionnaire. Re-absorption of phosphate by the proximal renal tubule, phosphate clearance and renal threshold phosphate concentration were the main outcome measures in both groups. Of the 87 patients with chronic fatigue syndrome, nine also fulfilled the diagnostic criteria for phosphate diabetes. In conclusion, we report a previously undefined relationship between chronic fatigue syndrome and phosphate diabetes. Phosphate diabetes should be considered in differential diagnosis with chronic fatigue syndrome; further studies are needed to investigate the incidence of phosphate diabetes in patients with chronic fatigue syndrome and the possible beneficial effect of vitamin D and oral phosphate supplements.</p>
<p>De Lorenzo F, Xiao H, Mukherjee M, Harcup J, Suleiman S, Kadziola Z, Kakkar VV.</p>	<p>Thrombosis Research Institute, London, UK.</p>	<p>Chronic fatigue syndrome: physical and cardiovascular deconditioning.</p>	<p>QJM 1998 Jul;91(7):475-81</p>	<p>We investigated whether chronic fatigue syndrome (CFS) patients have physical and/or cardiovascular deconditioning, in 273 CFS patients and 72 healthy controls. We used laboratory tests to assess haematological, biochemical, endocrinological and immunological systems. The cardiovascular system was assessed by echocardiography and carotid echography. Body composition was determined by dual energy X-ray absorptiometry (DEXA). CFS patients had smaller left ventricular end systolic ($p < 0.001$) and diastolic ($p = 0.008$) dimensions but thinner posterior walls ($p = 0.02$) than corresponding values in healthy controls. Left ventricular mass was also reduced in CFS patients ($p = 0.006$). Both maximum ($p < 0.001$) and minimum ($p < 0.008$) diameter of the carotid artery were smaller in CFS patients. The laboratory screening tests showed significant differences in serum albumin ($p = 0.05$), phosphate ($p = 0.02$), HDL-cholesterol ($p = 0.03$), HDL:total cholesterol ratio ($p = 0.01$), triglycerides ($p = 0.02$), neutrophils ($p = 0.01$) and thyroid-stimulating hormone ($p = 0.04$) between CFS patients and controls. Male CFS patients had an increased percentage of fat mass compared with healthy male subjects ($p = 0.02$). This large group of CFS patients had evidence of physical and cardiovascular de-conditioning, suggesting that in these patients a graded exercise programme could lead to physical reconditioning and could increase their ability to perform physical activities.</p>
<p>Deale A, Chalder T, Wessely S.</p>	<p>Department of Psychological Medicine, Kings College Hospital, and Institute of Psychiatry, London, UK.</p>	<p>Illness beliefs and treatment outcome in chronic fatigue syndrome.</p>	<p>J Psychosom Res 1998 Jul;45(1 Spec No):77-83</p>	<p>Longitudinal studies have shown that physical illness attributions are associated with poor prognosis in chronic fatigue syndrome (CFS). Speculation exists over whether such attributions influence treatment outcome. This study reports the effect of illness beliefs on outcome in a randomized controlled trial of cognitive-behavior therapy versus relaxation. Causal attributions and beliefs about exercise, activity, and rest were recorded before and after treatment in 60 CFS patients recruited to the trial. Physical illness</p>

				attributions were widespread, did not change with treatment, and were not associated with poor outcome in either the cognitive-behavior therapy group or the control group. Beliefs about avoidance of exercise and activity changed in the cognitive behavior therapy group, but not in the control group. This change was associated with improved outcome. These findings suggest that physical illness attributions are less important in determining outcome (at least in treatment studies) than has been previously thought. In this study, good outcome is associated with change in avoidance behavior, and related beliefs, rather than causal attributions.
Deale A, Chalder T, Wessely S.	Department of Psychological Medicine, King's College Hospital, London.	Commentary on: Randomised, double-blind, placebo-controlled trial of fluoxetine and graded exercise for chronic fatigue syndrome.	Br J Psychiatry 1998 Jun;172:491-2 Comment on: Br J Psychiatry. 1998 Jun;172 :485-90	
Delbanco TL, Daley J, Hartman EE.		A 56-year-old woman with chronic fatigue syndrome, 1 year later.	JAMA 1998 Jul 22-29;280(4):372 Comment on: JAMA. 1997 Oct 8;278(14):1179-85	
Demitrack MA, Crofford LJ.	Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, Indiana 46285, USA.	Evidence for and pathophysiologic implications of hypothalamic-pituitary-adrenal axis dysregulation in fibromyalgia and chronic fatigue syndrome.	Ann N Y Acad Sci 1998 May 1;840:684-97	Chronic fatigue syndrome (CFS) is characterized by profound fatigue and an array of diffuse somatic symptoms. Our group has established that impaired activation of the hypothalamic-pituitary-adrenal (HPA) axis is an essential neuroendocrine feature of this condition. The relevance of this finding to the pathophysiology of CFS is supported by the observation that the onset and course of this illness is exacerbated by physical and emotional stressors. It is also notable that this HPA dysregulation differs from that seen in melancholic depression, but shares features with other clinical syndromes (e.g., fibromyalgia). How the HPA axis dysfunction develops is unclear, though recent work suggests disturbances in serotonergic neurotransmission and alterations in the activity of AVP, an important co-secretagogue that, along with CRH, influences HPA axis function. In order to provide a more refined view of the nature of the HPA disturbance in patients with CFS, we have studied the detailed, pulsatile characteristics of the HPA axis in a group of patients meeting the 1994 CDC case criteria for CFS. Results of that work are consistent with the view that patients with CFS have a reduction of HPA axis activity due, in part, to impaired central nervous system drive. These observations provide an important clue to the development of more effective treatment to this disabling condition.
Demitrack MA.	Lilly Research Laboratories, Indianapolis, Indiana, USA.	Chronic fatigue syndrome and fibromyalgia. Dilemmas in diagnosis and clinical management.	Psychiatr Clin North Am 1998 Sep;21(3):671-92, viii	There has been a resurgence of interest in recent years in both chronic fatigue syndrome and fibromyalgia. These perplexing and common clinical conditions are a source of significant patient morbidity and frame one of the more enduring dilemmas of contemporary Western medical thought, namely the ambiguous interface between mind and body. In this article, the current definitions are reviewed, and a framework for an emerging psychobiological model of these syndromes is presented. These issues are synthesized into a pragmatic approach to clinical management. Review, Academic
Demitrack MA.	Lilly Research Laboratories, Neuroscience Therapeutic Area, Indianapolis, Indiana 46285, USA.	Neuroendocrine aspects of chronic fatigue syndrome: a commentary.	Am J Med 1998 Sep 28;105(3A):11S-14S	
Devitt NF.		Chronic fatigue syndrome.	JAMA 1998 Feb 11;279(6):432; discussion 432-3 Comment on: JAMA. 1997 Oct 8;278(14):1179-85	
Duprez DA, De Buyzere ML, Drieghe B, Vanhaverbeke F, Taes Y, Michielsens W, Clement DL.	Department of Cardiology and Angiology, University Hospital, Gent, Belgium.	Long- and short-term blood pressure and RR-interval variability and psychosomatic distress in chronic fatigue syndrome.	Clin Sci (Colch) 1998 Jan;94(1):57-63 Comment in: Clin Sci (Colch). 1999 Sep;97(3):319-22	1. Chronic low blood pressure has been associated with fatigue and low mood. However, in the chronic fatigue syndrome (CFS) the blood pressure (BP) and heart rate profile and their variabilities have not been characterized as yet. 2. We performed office and 24 h ambulatory BP recordings in 38 subjects (age, 34.8 8.0 years) who fulfilled the Holmes criteria for CFS and in 38 healthy control subjects (age 35.6 10.5 years), as well as short-term beat-to-beat BP and RR-interval recordings for 10 min in supine and standing position, and calculated spectral indices. 3. In CFS office (123 19/70 12 mmHg) as well as 24-h, day- and night-time blood pressure values (116 11.1/71 11.1, 121 9.2/77 8.0 and 110 10.5/65 9.2 mmHg

				respectively) were within reference limits. 4. Heart rate was consistently higher ($P < 0.01$) in CFS patients, based on both office (77 12 compared with 68 12 beats min ⁻¹) and 24 h ambulatory recordings (77 12 compared with 67 15 beats min ⁻¹). 5. In supine position, spectral indices of BP variability (total, low-frequency and high-frequency variances) were all significantly ($P < 0.01$) lower in CFS. In standing position the differences disappeared. Analysis of RR-interval variability could not detect major alterations in autonomic function in CFS.
Dykman KD, Tone C, Ford C, Dykman RA.	Mannatech Inc., Coppell Texas 75019, USA.	The effects of nutritional supplements on the symptoms of fibromyalgia and chronic fatigue syndrome.	Integr Physiol Behav Sci 1998 Jan-Mar;33(1):61-71	This article reports the results of a within-subject design. Fifty subjects with a physician diagnosis of fibromyalgia (FM) and/or chronic fatigue syndrome (CFS) were interviewed using a structured interview from. Each subject was interviewed initially, and again nine months later (follow-up). Subjects had, on their own, consumed nutritional supplements including freeze-dried aloe vera gel extract; a combination of freeze-dried aloe vera gel extract and additional plant-derived saccharides; freeze-dried fruits and vegetables in combination with the saccharides; and a formulation of dioscorea complex containing the saccharides and a vitamin/mineral complex. With medical treatments, approximately 25 percent of FM patients improve, but the beneficial effects of medical treatment rarely persist more than a few months. All subjects in this study had received some form of medical treatment prior to taking the nutritional supplements, but none with enduring success. Nutritional supplements resulted in a remarkable reduction in initial symptom severity, with continued improvement in the period between initial assessment and the follow-up. Further research is needed to verify these results, specifically crossover designs in well-defined populations.
Empson M.		Celiac disease or chronic fatigue syndrome--can the current CDC working case definition discriminate?	Am J Med 1998 Jul;105(1):79-80	
Endicott NA		Chronic Fatigue Syndrome in Psychiatric Patients: Evidence of Premorbid Anomalous Patterns of Brain Organization	Journal of Chronic Fatigue Syndrome 1998; 5(1): 29 - 45	Forty-six patients with chronic fatigue syndrome (CFS) were matched with two control groups: one chosen on the basis of relatively good physical health (N = 92) and the other without regard to physical health (N = 46). All patients were from the same psychiatric practice. The groups were compared on 20 anomalous brain conditions or phenomena (ABCP) used as markers of patterns of brain organization. The results suggest that psychiatric patients who subsequently develop CFS have a higher number of pre-CFS ABCP, of both childhood and adult onset, than psychiatric patients who have not developed this condition
Endicott NA.	Department of Research Assessment and Training, New York State Psychiatric Institute, New York, USA.	Chronic fatigue syndrome in psychiatric patients: lifetime and premorbid personal history of physical health.	Psychosom Med 1998 Nov-Dec;60(6):744-51	OBJECTIVE: This preliminary report compares a group of chronic fatigue syndrome (CFS) patients and controls on several variables of potential significance in the etiology of CFS. METHOD: The lifetime prevalence of reported physical disorders was compared among 46 CFS psychiatric patients, 92 relatively physically healthy psychiatric patients (C-I), and 46 psychiatric patients selected without regard to physical health (C-II). All patients were matched on age, sex, and psychiatric diagnosis and were drawn from the same psychiatric practice. The same groups were compared on a 7-point scale of lifetime physical health by three raters independently evaluating physical health narratives of the CFS patients up to the time of onset of CFS and that of the controls up to the corresponding age. RESULTS: The CFS patients had a significantly higher reported lifetime prevalence of irritable bowel syndrome (IBS), infectious mononucleosis-like syndromes (IM), infectious mononucleosis-like syndromes two or more times (IM x 2), and herpes (other than genital or perioral herpes) than one or both control groups. The CFS group also had a higher incidence of allergic rhinitis or asthma, IBS, IM, and IM x 2 than the combined controls. On the independent ratings, the CFS patients had significantly more impaired physical health up to the time of onset of the CFS than C-I at a comparable age. CONCLUSIONS: The findings suggest that a general health factor may be involved in the pathogenesis of some cases of CFS.
Essame CS, Sue Phelan, Percy Aggett Peter D. White		Pilot Study of a Multidisciplinary Inpatient Rehabilitation of Severely Incapacitated Patients with the Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998; 4(2): 51 - 60	The outcome of severely incapacitated patients with the chronic fatigue syndrome is poor. We examined the outcome of the first 19 such patients admitted to a psychiatric ward in a general hospital for a multidisciplinary rehabilitation programme. Seventeen (89%) patients had functionally improved by discharge, the median Karnofsky score improvement being 15 points in all 19 patients. All fourteen patients who were followed up had maintained or exceeded their improvement by one year, with a median Karnofsky score improvement of 25 in all 16 followed up patients, compared to admission. Only two patients had not improved by discharge and they were the same or worse at one year. A randomised controlled trial is necessary to confirm the efficacy and acceptability of this form of rehabilitation.

Evengard B, Nilsson CG, Lindh G, Lindquist L, Eneroth P, Fredrikson S, Terenius L, Henriksson KG.	Department of Infectious Diseases, Karolinska Institute at Huddinge Hospital, Stockholm, Sweden.	Chronic fatigue syndrome differs from fibromyalgia. No evidence for elevated substance P levels in cerebrospinal fluid of patients with chronic fatigue syndrome.	Pain 1998 Nov;78(2):153-5	Levels of substance P were determined in the cerebrospinal fluid (CSF) in 15 patients with chronic fatigue syndrome (CFS). All values were within normal range. This is in contrast to fibromyalgia (FM). The majority of patients with FM have increased substance P values in the CSF. The results support the notion that FM and CFS are different disorders in spite of overlapping symptomatology.
Findley JC, Kerns R, Weinberg LD, Rosenberg R.	V.A. Connecticut Healthcare System, West Haven 06516, USA.	Self-efficacy as a psychological moderator of chronic fatigue syndrome.	J Behav Med 1998 Aug;21(4):351-62	Chronic fatigue syndrome (CFS) is characterized by debilitating fatigue and a variety of somatic symptoms. Few studies have examined psychological aspects of CFS. In the present study, self-efficacy is shown to be a significant predictor of CFS symptoms beyond the variance accounted for by demographic variables and distress. Further psychological CFS research is encouraged by (1) identifying dimensions that are salient in the experience and study of CFS, (2) providing preliminary psychometric data for measures of those dimensions, and (3) identifying psychological variables that serve as moderators of the experience of CFS.
Fischler B, Patrick Flamen Hendrik Everaert Axel Bossuyt Kenny De Meirleir		Physiopathological Significance of 99mTc HMPAO SPECT Scan Anomalies in Chronic Fatigue Syndrome A Replication Study	Journal of Chronic Fatigue Syndrome 1998; 4(4): 15 - 30	Regional cerebral blood flow as measured by 99mTc HMPAO SPECT imaging was compared between chronic fatigue syndrome (CFS) and healthy controls (HC). Larger right(R) > left(L) asymmetry at the parietotemporal level in CFS as compared to HC was observed in accordance with several previous studies. On the contrary, in most regions of interest, hypoperfusion was not confirmed in CFS, and hyperperfusion was demonstrated in several frontal and temporal regions. No significant correlations were found between frontal tracer uptake and R-L parietotemporal asymmetry, on the one hand, and clinically relevant CFS dimensions, on the other.
Franklin A.		How I manage chronic fatigue syndrome.	Arch Dis Child 1998 Oct;79(4):375-8	
Fuller NS, Morrison RE.	Division of General Internal Medicine, University of Tennessee, College of Medicine, Memphis 38103, USA.	Chronic fatigue syndrome. Helping patients cope with this enigmatic illness.	Postgrad Med 1998 Jan;103(1):175-6, 179-84	Chronic fatigue syndrome is a recurring, debilitating illness complicated by the fact that its diagnosis is largely based on subjective complaints and the absence of reproducibly reliable tests. There is no known "cure" for this illness; however, in general, the prognosis for patients is good. Some physicians accept the existence of chronic fatigue syndrome, while others are convinced that it exists only in the minds of its "victims." The majority of physicians, however, are skeptical but open-minded and wish to help their chronically fatigued patients. As more information comes to light, it is likely that modern medicine will have to rethink its views on this elusive illness. In the interim, patients with chronic fatigue syndrome need the support and reassurance of their physicians to help them cope with their symptoms and resume normal, productive lives.
Garcia-Borreguero D, Dale JK, Rosenthal NE, Chiara A, O'Fallon A, Bartko JJ, Straus SE.	Clinical Psychobiology Branch, National Institute of Mental Health, Bethesda, MD 20892, USA.	Lack of seasonal variation of symptoms in patients with chronic fatigue syndrome.	Psychiatry Res 1998 Feb 9;77(2):71-7	Several of the symptoms involved in chronic fatigue syndrome (CFS) such as fatigue, hypersomnia, hyperphagia, weight gain, and mood show seasonal variations in the general population. The aim of this study was to investigate whether patients with CFS experience seasonal fluctuations in these symptoms as well. Seasonal variation of symptoms was assessed in a group of 41 patients with CFS and 41 controls closely matched for age, gender, and city of residence. Participants were recruited across the US and were asked to complete the Seasonal Pattern Assessment Questionnaire (SPAQ) and the Profile of Mood States (POMS). CFS patients showed significantly lower scores on multiple SPAQ-derived measures as compared with controls. These included seasonal variation in energy, mood, appetite, weight, and sleep length. Patients also reported a significantly reduced sensitivity toward sunny, dry, and long days than controls. No association was noted between intensity of seasonal changes and severity of depressive symptoms. Patients with CFS exhibit an abnormally reduced seasonal variation in mood and behavior and would not be expected to benefit from light therapy.
Gibbons, Pheby , C. Richards , F. I. Bray		Severe CFS/ME of Juvenile Onset- A Report from the CHROME Database	Journal of Chronic Fatigue Syndrome 1998; 4(4): 67 - 80	CHROME has been collecting data since 1995 on very severely disabled patients in the UK with ME, in order to assess aspects of physical and cognitive levels of disability at the onset of the illness and to monitor progress. Results of the first two years data (225 cases) collection are reported. The modal age of onset for this severe group of patients was 11-15, and the proportion increased with more recent years of onset. Patients tended to deteriorate between onset and recruitment in cognitive and functional ability, and in sensory and sleep disturbance. Statistical significance was assessed using McNemar's Test for comparing correlated proportions.
Gimenez HB, P. Cash, R. B. S. Laing, J. G. Douglas		Cytokine Expression and Morphology of in vitro	Journal of Chronic Fatigue Syndrome 1998; 5(1): 47 - 60	Although the underlying metabolic cause of chronic fatigue syndrome (CFS) is unknown, specific defects have been proposed to exist in the skeletal muscle, the immune system and the neuroendocrine system.

		Grown Monocytes from Patients with Chronic Fatigue Syndrome		Peripheral blood mononuclear cells from CFS patients and healthy controls were fractionated as adherent cells (monocyte-enriched fraction) and non-adherent cells. We have investigated some activities of the former during in vitro culture. It was observed that the morphology (shape and size) of adherent cells from CFS patients, cocultivated with homologous non-adherent cells, differed between CFS patients and healthy controls for 21 out of 25 (84%) paired samples (i.e., CFS patient and healthy control). Cytokine expression was examined for the adherent cell population collected from 14 CFS patients and 12 healthy controls. Unstimulated and LPS stimulated tumour necrosis factor- α (TNF α) expression was higher for monocytes from 7 out of 14 CFS patients. Unstimulated interleukin-1 β (IL-1 β) expression was higher for monocytes from 10 out of 14 CFS patients, whereas LPS-stimulated IL-1 β expression was higher for 8 out of 14 CFS patients. The proportional increase of IL-1 β and TNF α following LPS stimulation was lower for the majority of the CFS patients studied, suggesting that the monocytes from CFS patients were less responsive to LPS than the respective healthy controls. The basis for the abnormal in vitro monocyte maturation, the elevated unstimulated levels of IL-1 β expression and the abnormal response of the monocytes to LPS is unknown. The relevance of these findings to CFS pathogenesis is discussed
Glaser R, Kiecolt-Glaser JK.	Department of Medical Microbiology and Immunology, Comprehensive Cancer Center, The Ohio State University College of Medicine, Columbus 43210, USA.	Stress-associated immune modulation: relevance to viral infections and chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):35S-42S	The frequent association of an active viral infection with the symptoms of CFS led researchers to hypothesize that chronic fatigue syndrome (CFS) is induced by a virus. Results of these studies indicated that despite clinical support for this hypothesis, there were no clear data linking viruses to CFS. In this overview, we will explore the interrelation of the immune, endocrine, and central nervous systems, and the possibility that stress and/or the reactivation/replication of a latent virus (such as Epstein Barr virus) could modulate the immune system to induce CFS. Relevant research conducted in the developing field of psychoneuroimmunology will be reviewed, with a particular focus on cytokine synthesis, natural killer (NK) cell activity, and T-lymphocyte function, as they relate to CFS.
Goshorn RK.	Department of Internal Medicine, Indiana University Hospital, Indianapolis, USA.	Chronic fatigue syndrome: a review for clinicians.	Semin Neurol 1998;18(2):237-42	Syndromes characterized by persistent fatigue, musculoskeletal pain, sleep disturbance, and subjective cognitive impairment have been common problems in clinical practice for decades. The chronic fatigue syndrome case definition was created to standardize the patient population in research studies and to foster a systematic and comprehensive approach to the attempt to define the etiology and pathophysiology of these syndromes. The pathogenesis of chronic fatigue syndrome remains unknown, though it does appear to be associated with subtle neuroendocrine and immunologic abnormalities. Treatment of chronic fatigue syndrome is empirical. Significant palliation is often possible, though treatment success requires skillful practice of the art of medicine.
Hall GH, Hamilton WT, Round AP.		Increased illness experience preceding chronic fatigue syndrome.	J R Coll Physicians Lond 1998 Jul-Aug;32(4):389 Comment on: J R Coll Physicians Lond. 1998 May-Jun;32(3):274	
Hall GH, Hamilton WT, Round AP.		Increased illness experience preceding chronic fatigue syndrome: a case control study.	J R Coll Physicians Lond 1998 Jan-Feb;32(1):44-8 Comment in: J R Coll Physicians Lond. 1998 May-Jun;32(3):274	BACKGROUND: Almost all published work on chronic fatigue syndrome (CFS) has involved retrospective surveys of cases, which may introduce recall bias. Only medical records collected before diagnosis of CFS can eliminate this. METHODS: Using data collected several years prior to the development of the illness, we performed a case control study, comparing the reported illness records of all people who subsequently made an insurance claim as a result of CFS, with those of future multiple sclerosis (MS) claimants, and those of non-claimant controls (NC). RESULTS: The study encompassed 133 CFS, 75 MS and 162 NC cases. CFS cases had recorded significantly more illnesses at time of proposal for insurance than the two control groups, and had significantly more claims between proposal and diagnosis of their disorder. Almost all disease categories were reported higher in future CFS sufferers, lethargy having the highest odds ratio after adjustment in a multivariate model. INTERPRETATION: The results of this paper on CFS patients who claim permanent health insurance do not support a specific viral or immunological explanation for CFS. We conclude that abnormal illness behaviour is of greater importance than previously recognised.
Hamilos DL, Nutter D, Gershtenson J, Redmond DP, Clementi JD, Schmalig KB, Make BJ, Jones JF.	National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado, USA.	Core body temperature is normal in chronic fatigue syndrome.	Biol Psychiatry 1998 Feb 15;43(4):293-302	BACKGROUND: Subjects with chronic fatigue syndrome (CFS) frequently report symptoms of subnormal body temperature and low-grade fever. We conducted a study to determine whether CFS subjects manifest any abnormality of core body temperature (CBT) that might help explain their fatigue. METHODS: Continuous 24-hour recordings of CBT measured every 5 min were performed in 7 subjects meeting the Centers for Disease Control definition of CFS. Three additional groups were studied: normal controls,

				<p>subjects with seasonal allergy, and subjects with major depression. Subjects (n = 7) in each group were age-, sex-, and weight-matched to the CFS group and had normal basal metabolic rates, thyroid function, and 24-hour urinary free cortisol excretions. CBT was measured with an ingestible radio frequency transmitter pill and a belt-worn receiver-logger. Each pill was factory-calibrated to 0.1 degree C and field-calibrated with a water bath calibration prior to use. RESULTS: The 24-hour mean calibration-adjusted CBTs of each group were not significantly different (control: 37.00 ± 0.17 degrees C; CFS: 37.04 ± 0.31 degrees C; allergy: 37.15 ± 0.18 degrees C; depression: 37.16 ± 0.18 degrees C). Similarly, the mean peak and trough circadian temperatures were not statistically different. The mean 24-hour profile of CBT for each group showed a similar circadian rhythm. In simultaneously collected blood samples, each group showed a similar circadian profile of serum cortisol with a peak occurring at 08:00. CONCLUSIONS: Subjects with CFS have normal CBT despite frequent self-reports of subnormal body temperature and low-grade fever.</p>
<p>Harlow BL, Signorello LB, Hall JE, Dailey C, Komaroff AL.</p>	<p>Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.</p>	<p>Reproductive correlates of chronic fatigue syndrome.</p>	<p>Am J Med 1998 Sep 28;105(3A):94S-99S</p>	<p>A case-control study was conducted to determine whether menstrual and gynecologic abnormalities precede the onset of chronic fatigue syndrome (CFS) in women with this disorder to a greater extent than that observed among healthy controls. We identified 150 women who met the 1988 Centers for Disease Control criteria for CFS from the Brigham and Women's Hospital Cooperative CFS Research Center. A comparison group of 149 women being seen for nongynecologic conditions were selected from the waiting area of the Brigham and Women's Hospital Internal Medicine outpatient department. Women with and without CFS completed self-administered questionnaires on menstrual, reproductive, and medical history. Women with CFS reported increased gynecologic complications and a lower incidence of premenstrual symptomatology. After adjustment for age, a somewhat greater number of cases compared with controls self-reported irregular cycles, periods of amenorrhea, and sporadic bleeding between menstrual periods. Factors suggestive of abnormal ovarian function--such as a history of polycystic ovarian syndrome, hirsutism, and ovarian cysts--were reported more often in CFS cases compared with controls. Frequent anovulatory cycles due to ovarian hyperandrogenism (PCOS) or hyperprolactinemia may increase risk for CFS through loss of the potential immunomodulatory effects of progesterone in the presence of continued estrogen production. We hypothesize that frequent anovulatory cycles due to PCOS and/or hyperprolactinemia may explain the increased reporting of gynecologic complications and the lower reported premenstrual symptomatology observed in women with CFS.</p>
<p>Harrigan P.</p>		<p>Controversy continues over chronic fatigue syndrome.</p>	<p>Lancet 1998 Feb 21;351(9102):574 Comment in: Lancet. 1998 Apr 25;351(9111):1292</p>	
<p>Hartz AJ, Evelyn M. Kuhn, Paul H. Levine</p>		<p>Characteristics of Fatigued Persons Associated with Features of Chronic Fatigue Syndrome</p>	<p>Journal of Chronic Fatigue Syndrome 1998; 4(3): 71 - 97</p>	<p>Background: Characteristics of persons with chronic fatigue syndrome (CFS) have previously been studied by comparing subjects with CFS to subjects with other conditions or no symptoms of fatigue. In the present study of subjects with idiopathic chronic fatigue we examined the association between the number and severity of the features of CFS with other characteristics of the subjects. Methods: Data were obtained from a registry of persons over the age of 17 with fatigue for at least six months. All subjects in the registry completed an extensive questionnaire that provided information about fatigue, demographic characteristics, medical conditions, life style, sleeping habits, and psychological characteristics. The characteristics of the subjects were tested for an association with the number of CFS symptoms and the severity of individual CFS symptoms that are considered to be of fundamental importance and may identify more homogeneous subjects with chronic fatigue. Results: The number of CFS symptoms had a bell shaped distribution. This number was strongly associated with the severity of fatigue, the response of fatigue to mental and physical activity, and the following subject characteristics: a greater frequency of sinus and respiratory infections, a higher frequency of migraine headaches, a greater number of somatoform symptoms that were not included as criteria for CFS, and not drinking alcohol. These same subject characteristics were generally associated with at least one of the individual CFS symptoms but more weakly. Psychological complaints only had a statistically significant positive association with one feature of CFS, neurocognitive complaints. Conclusions: Persons with fatigue can be usefully characterized by the extent to which they meet the CFS criteria.</p>
<p>Hassan IS, Bannister BA, Akbar A, Weir W, Bofill</p>	<p>Department of Infectious & Tropical Diseases, Royal</p>	<p>A study of the immunology of the chronic fatigue</p>	<p>Clin Immunol Immunopathol 1998 Apr;87(1):60-7</p>	<p>Surface and intracellular immunologic and apoptotic markers and functional lymphocyte assays after stimulation with anti-CD3/anti-CD28 antibodies or phytohemagglutinin (PHA) were studied in 44 patients</p>

M.	Free Hospital, London, England.	syndrome: correlation of immunologic parameters to health dysfunction.		fulfilling the Oxford criteria for chronic fatigue syndrome (CFS). Results were then correlated to scores for the Short Form-36 health questionnaire (SF-36), which assesses eight aspects of patient's well-being, and for the general health questionnaire (GHQ), which detects current psychiatric disorder. Patients had significantly increased mean fluorescence intensity readings of HLA-DR in CD4 and CD8 cells ($P < 0.05$). Expression of the costimulatory receptor CD28 in CD8 cells was significantly reduced, and the apoptosis repressor ratio of bcl-2/bax in both CD4 and CD8 was increased in patients ($P < 0.05$). Patients with increased HLA-DR expression had significantly lower SF-36 total scores, worse body pains, and poorer general health perception and physical functioning scores. Increased spontaneous lymphocyte proliferation was associated with poor general health perception. PHA proliferative responses were lower in patients with poor emotional and mental health scores, and the anti-CD3/anti-CD28 response was low in those with low general health perception scores. Higher spontaneous proliferation and reduced PHA responses correlated with higher GHQ scores. Similarly, GHQ scores were significantly higher, indicating worse mental health, in those with lower total SF-36 scores and worse general and mental health scores in the SF-36 questionnaire. Finally, higher expression of the costimulatory molecule CD28 correlated with higher total SF-36 scores, general health perception and social functioning scores, and with lower role limitation due to physical health. The increased expression of class II antigens and the reduced expression of the costimulatory receptor CD28, which is a marker of terminally differentiated cells, lend further support to the concept of immunoactivation of T-lymphocytes in CFS and may be consistent with the notion of a viral etiopathogenesis in the illness. We report, for the first time, increased expression of the apoptosis repressor protein bcl-2, which may contribute to enhanced survival of activated lymphocytes. Using the SF-36 health assessment questionnaire and the GHQ, we demonstrated changes in different immunological parameters, each of which correlated with particular aspects of disease symptomatology.
Heijmans M, de Ridder D.	Department of Health Psychology, Utrecht University, The Netherlands.	Assessing illness representations of chronic illness: explorations of their disease-specific nature.	J Behav Med 1998 Oct;21(5):485-503	Elaborating on the five-dimensional structure of illness representation, as described in the self-regulation model of Leventhal (1980), the present study is aimed at identifying the relevance of this generic structure for two chronic illnesses: chronic fatigue syndrome (CFS) and Addison's disease (AD). Factor analyses showed the importance of the five dimensions identity, time-line, control/cure, cause, and consequences to differ according to the type of disease. That is, the items representing the five dimensions merged together for CFS patients and AD patients in a different manner and thereby produced different factor solutions for the two patient groups. In CFS patients, a four-factor solution was identified with manageability, seriousness, personal responsibility, and external cause as the factors. In AD patients a four-factor solution was also identified but with seriousness, cause, chronicity, and controllability as the factors. The value of these findings for our understanding of the disease-specific nature of illness representation is discussed.
Heijmans MJ.	Department of Clinical and Health Psychology, Utrecht University, The Netherlands. M.Heijmans@fsw.ruu.nl	Coping and adaptive outcome in chronic fatigue syndrome: importance of illness cognitions.	J Psychosom Res 1998 Jul;45(1 Spec No):39-51	In this study, the relations between illness representations, coping behavior, and adaptive outcomes in chronic fatigue syndrome (CFS) patients (N=98) were examined. Following Leventhal's self-regulation model, it was hypothesized that illness representations would be directly related to coping and, via coping, to adaptive outcome. The results showed patients who considered their illness to be a serious condition, who believed that they had no control over their illness, who saw little possibility for cure, and who believed their illness to have serious consequences to cope with their illness in a passive way, report higher levels of impairment in physical and social functioning and report greater problems in mental health and vitality. A series of regression analyses showed illness representations to be stronger predictors of adaptive outcome than coping scores. The implications of these findings for the treatment of CFS patients are discussed.
Heller U, Becker EW, Zenner HP, Berg PA.	HNO-Klinik, Universitat Tubingen.	[Incidence and clinical relevance of antibodies to phospholipids, serotonin and ganglioside in patients with sudden deafness and progressive inner ear hearing loss]. [article in German]	HNO 1998 Jun;46(6):583-6 Comment in: HNO. 1998 Jun;46(6):565-6	Immunoserological assays of patients with sudden deafness and progressive hearing losses have revealed the presence of different antibodies, leading to the assumption that immunological processes may be involved. Recent investigations have demonstrated that these patients have phospholipid antibodies that can cause venous or arterial vasculopathies. In the present study we analyzed the incidence of these antibodies in patients with inner ear disorders. Sera of 55 patients with sudden deafness and 80 patients with progressive hearing loss were tested. Phospholipid antibodies were demonstrable in 49% of the patients with sudden hearing loss and 50% of the patients with progressive hearing loss. Serotonin and ganglioside antibodies were found in 53% of the patients with sudden hearing loss and 63% of the patients with progressive hearing loss. Since these three antibodies are also frequently found in patients with fibromyalgia syndrome (FMS) and chronic fatigue syndrome (CFS), 28 of the patients studied displayed

				symptoms typical for these disorders, including fatigue, myalgia, arthralgia, depressions, sicca symptoms and diarrhea. We now recommend questioning patients suffering from inner ear disorders for symptoms typical for FMS or CFS, since these diseases are often closely related to inner ear disorders. If symptoms are present, antibodies should be tested against phospholipids, serotonin and gangliosides. If present, the antibodies are diagnostic for each syndrome. Additionally these immunologic and serologic findings show that these antibodies may play a role in the etiology of hearing loss disorders.
Hicks MH, Kleinman A, Yang L.	Department of Social Medicine, Harvard Medical School, Boston, USA.	The social course of schizophrenia: local and societal factors.	Kaohsiung J Med Sci 1998 Jul;14(7):432-47	In this paper, we propose a model of social course of schizophrenia based on cross-cultural research on the influence of family, wider social network, work, political economy, and legal and mental health care institutions on the experience of illness. We posit the way these ordinary arrangements of daily living organize the course of schizophrenia in part through cultural processes that affect the body-self in suffering and in part through social processes that establish an intersubjective matrix for the experience of illness. We believe this model can be generalized to other chronic illness such as depression, diabetes, asthma, osteoarthritis, chronic pain syndrome, chronic fatigue syndrome, and even heart disease and cancer. We develop the implications of this anthropological approach for research and practice.
Hilgers A, Johannes Frank, Petra Bolte		Prolongation of Central Motor Conduction Time in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998; 4(2): 23 - 32	We compared the central motor conduction time (CMCT) obtained by magnetic stimulation of the central nervous system (CNS) of 181 patients who fulfilled the criteria (see Fukuda 1994) for CFS with those of 27 healthy control subjects. A cortical and a cervical stimulation was performed on each person under standardised conditions, and the motor evoked potentials (MEP) either from Musculus Abductor Pollicis Brevis (M. APB) or from Musculus Abductor Digiti Minimi (M. ADM) was recorded. For the CFS patients a significant prolongation of the central motor conduction time (M. APB right: $p < 0.0001$; M. ADP left: $p < 0.00005$; M. ADM right: $p < 0.00005$; M. ADM left: $p < 0.005$) was observed compared to controls. The results presented in this study suggest a central nervous system dysfunction in CFS.
Hyman H, Thomas E. Wasser		Gastrointestinal Manifestations of Chronic Fatigue Syndrome (CFS) Symptom Perceptions and Quality of Life	Journal of Chronic Fatigue Syndrome 1998; 4(1): 43 - 52	Objectives: This study examines the differences in symptoms and Quality of Life (QOL) among patients presenting to a gastrointestinal (GI) service with combinations of chronic fatigue syndrome (CFS) and GI complaints. Methods: We conducted a clinical examination of patients from a private GI practice and divided them into three groups: A combination group consisting of patients diagnosed with both CFS and functional bowel disease (FBD) (Group 1, $n = 5$); those positively diagnosed with CFS, who also reported GI symptoms, but without a prior GI diagnosis (Group 2, $n = 6$); and those with FBD, but without a diagnosis of CFS (Group 3, $n = 11$). These groups were prospectively surveyed, using the Medical Outcomes Study Short Form-36 (SF-36) and the Symptom Index Survey (SIS). Results: Data indicate CFS patients report more symptoms than non-CFS patients, as measured by the SIS, in these areas: Allergies, Digestive Tract, Ears, Eyes, Head, Immune, Joints/Muscles and Metabolism/Endocrine. SF-36 data indicated lower QOL for CFS patients compared to FBD alone (Group 3) patients in the General Health and Energy/Fatigue subscales. Conclusions: CFS patients with GI complaints demonstrate a significant relationship between both diagnoses. Since the observed differences occur between Groups 1 and 3, both with GI diagnoses, this indicates that these differences are a result of the presence or absence of CFS. Also, since these differences occur between CFS/ FBD and FBD-only, the classification of irritable bowel syndrome (IBS) should be modified to include a subset of patients who have a combination of CFS and IBS.
Jain SS, DeLisa JA.	Department of Physical Medicine and Rehabilitation, UMDNJ-New Jersey Medical School, Newark, USA.	Chronic fatigue syndrome: a literature review from a psychiatric perspective.	Am J Phys Med Rehabil 1998 Mar-Apr;77(2):160-7	To examine the literature on chronic fatigue syndrome (CFS), especially as it relates to cognitive deficits and exercise, more than 200 articles related to CFS were selected from computer-based research as well as pertinent articles noted in the references of individual articles. All were relevant articles on CFS, although articles in a foreign language were excluded. CFS is a controversial diagnosis of exclusion, but certain subgroups do appear to exist. It may represent multiple diseases or multiple stages of the same disease. Although cognitive deficits are commonly reported, the measured impairments are relatively subtle and are in the area of complex information processing speed, or efficiency. Magnetic resonance imaging, single-photon emission computer tomography, and neuroendocrine studies present preliminary evidence suggestive of the cerebral involvement primarily in the white matter. The weakness and fatigue may be the result of alterations in the central nervous system, not in the peripheral muscles. However, it is hard to separate the documented weakness and endurance deficits from deconditioning. Autonomic symptoms such as orthostatic intolerance and a predisposition to neurally mediated syncope may be explained by cardiovascular deconditioning, a postviral idiopathic autonomic neuropathy, or both. The review points out

				the need for more carefully designed studies of CFS that focus on the relationship between neuropathology, psychopathology and neuropsychologic functioning. The role of exercise as a stimulus for exacerbation or in treatment needs to be further studied using clear diagnostic criteria as well as control groups that carefully match the activity level.
Jason LA, Wagner L, Rosenthal S, Goodlatte J, Lipkin D, Papernik M, Plioplys S, Plioplys AV.	Department of Psychology, DePaul University, Northwestern Medical School, Rush Presbyterian--St. Luke's Medical Center, Chicago, Illinois 60614, USA.	Estimating the prevalence of chronic fatigue syndrome among nurses.	Am J Med 1998 Sep 28;105(3A):91S-93S	The present study assessed the prevalence of chronic fatigue syndrome (CFS) in a sample of nurses. There is a paucity of studies on the prevalence of CFS in healthcare professionals. Two samples of nurses were recruited through mailed questionnaires. Data were collected on demographic characteristics and symptoms. In addition from the sample, those nurses with CFS-like symptoms were more comprehensively evaluated using a structured clinical interview and reviewing their medical records. A physician review team estimated the prevalence of CFS to be 1,088 per 100,000. These findings suggest that nurses might represent a high-risk group for this illness, possibly due to occupational stressors such as exposure to viruses in the work setting, stressful shift work that is disruptive to biologic rhythms, or to other possible stressors in the work settings (e.g., accidents).
Jiaxu C, Yang Weiyi		Treatment of Chronic Fatigue Syndrome with Chinese Medicine	Journal of Chronic Fatigue Syndrome 1998; 5(1): 61 - 65	Chronic fatigue syndrome (CFS) is a severe, debilitating disorder, which prominently features self-reported impairments in concentration and short-term memory, and disturbances in sleep and emotions, all of which can affect any one and seriously affect quality of life. In 1987, the Centers for Disease Control and Prevention (CDC) defined CFS as persistent or relapsing fatigue, with at least 50% reduction of baseline activity level lasting for at least 6 months, as one of the main symptoms. Since its cause is still unknown, treatment of CFS has been palliative and has included usually orally administered products, such as vitamin B12, vitamin C, folic acid, iron, magnesium, essential fatty acids, coenzyme Q10 and nicotinamide adenine dinucleotide (NADH), among others. The latter therapeutic modalities can only relieve some symptoms to some extent, but cannot fundamentally eliminate fatigue. It is, therefore, urgent to seek safe and effective drugs for the treatment of fatigue. We propose here that regulating homeostasis and enhancing immunity are important for the treatment of fatigue. In China, many Chinese herbs with such functions have been proven effective, an observation which opens the possibility of a new therapeutic method of eliminating fatigue with traditional Chinese medicine (TCM).
Johnson SK.	Department of Psychology, University of North Carolina, 9201 University City Boulevard, Charlotte 28223-0001. skjohnso@email.uncc.edu.	The biopsychosocial model and chronic fatigue syndrome.	Am Psychol 1998 Sep;53(9):1080-2 Comment on: Am Psychol. 1997 Sep;52(9):973-83	
Jordan KM, Landis DA, Downey MC, Osterman SL, Thurm AE, Jason LA.	Department of Psychology, DePaul University, Chicago, Illinois 60614, USA.	Chronic fatigue syndrome in children and adolescents: a review.	J Adolesc Health 1998 Jan;22(1):4-18	
Joyce J, Rabe-Hesketh S, Wessely S.	Institute of Psychiatry, King's College School of Medicine, London, England.	Reviewing the reviews: the example of chronic fatigue syndrome.	JAMA 1998 Jul 15;280(3):264-6	OBJECTIVE: To test the hypothesis that the selection of literature in review articles is unsystematic and is influenced by the authors' discipline and country of residence. DATA SOURCES: Reviews in English published between 1980 and March 1996 in MEDLINE, EMBASE (BIDS), PSYCHLIT, and Current Contents were searched. STUDY SELECTION: Reviews of chronic fatigue syndrome (CFS) were selected. Articles explicitly concerned with a specialty aspect of CFS and unattributed, unreferenced, or insufficiently referenced articles were discarded. DATA EXTRACTION: Record of data sources in each review was noted as was the departmental specialty of the first author and his or her country of residence. The references cited in each index paper were tabulated by assigning them to 6 specialty categories, by article title, and by assigning them to 8 categories, by country of journal publication. DATA SYNTHESIS: Of 89 reviews, 3 (3.4%) reported on literature search and described search method. Authors from laboratory-based disciplines preferentially cited laboratory references, while psychiatry-based disciplines preferentially cited psychiatric literature (P = .01). A total of 71.6% of references cited by US authors were from US journals, while 54.9% of references cited by United Kingdom authors were published in United Kingdom journals (P = .001). CONCLUSION: Citation of the literature is influenced by review authors' discipline and nationality.
Kawakami N, Iwata N, Fujihara S, Kitamura T.	The Department of Public Health, Gifu University	Prevalence of chronic fatigue syndrome in a community	Tohoku J Exp Med 1998 Sep;186(1):33-41	In order to know the prevalence of chronic fatigue syndrome (CFS) in a community population in Japan, we analyzed data from a population-based interview survey. Two cases out of 137 respondents experienced

	School of Medicine, Japan. norito@cc.gifu-u.ac.jp	population in Japan.		chronic fatigue during a period of nine months, suffered from 50% or more reduction of daily activity due to fatigue and had no other physical or psychiatric diagnosis. Both of the two cases fulfilled the 1994 Centers for Disease Control (CDC) criteria and the British criteria. The point and nine-month prevalence rates of CFS were both 1.5% (95% confidence intervals, 0.4-5.2%). None fulfilled the 1989 CDC criteria for CFS. The prevalence rate of CFS was higher than those in previous studies in the Western countries, suggesting a need for future research on cross-cultural differences in the definition, prevalence and symptomatology of CFS.
Kenner C.	Department of Parent-Child Health Nursing, College of Nursing and Health University of Cincinnati, Ohio, USA.	Fibromyalgia and chronic fatigue: the holistic perspective.	Holist Nurs Pract 1998 Apr;12(3):55-63	Fibromyalgia syndrome (FMS) and chronic fatigue syndrome (CFS) are not new conditions, but they are receiving more attention as more research is conducted. These two conditions are primarily women's health problems. In some instances, there may be a genetic predisposition for these conditions. The impact of FMS and CFS can be devastating both physically and emotionally. The treatment plan must be interdisciplinary and holistic and include alternative therapies if the client and family are to be truly supported and helped in coping with these chronic conditions.
Klimas N.	University of Miami School of Medicine/VA Medical Center, Florida, USA.	Pathogenesis of chronic fatigue syndrome and fibromyalgia.	Growth Horm IGF Res 1998 Apr;8 Suppl B:123-6	
Klineberg I, McGregor N, Butt H, Dunstan H, Roberts T, Zerbes M.	Faculty of Dentistry, University of Sydney.	Chronic orofacial muscle pain: a new approach to diagnosis and management.	Alpha Omegan 1998 Jul;91(2):25-8	The initial data from this study indicate that there are clearly identifiable chronic muscle pain conditions in the form of localized pain; myofascial pain or regional pain conditions; and fibromyalgia or generalized pain conditions. A clear difference exists between the prevalence of these conditions in male and female patients, with a higher percentage of female patients suffering generalized pain problems and temporomandibular problems. Generalized or localized pain appears to be an individual variant of a similar problem and pain patients may have a genetically determined vulnerability associated with bacterial toxins, particularly within the genitourinary tract. It appears that in fibromyalgia there is an underlying genetic factor that causes abnormalities in the muscle metabolic cycle, and preliminary data suggest that lipid anomalies predispose to fibromyalgia and possibly chronic fatigue syndrome. Patients report infectious events at/or around onset in more than 60 percent of cases. Seventy percent of fibromyalgic cases report orofacial pain.
Komaroff AL, Buchwald DS.	Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.	Chronic fatigue syndrome: an update.	Annu Rev Med 1998;49:1-13	Among the many patients who seek medical care for the complaint of fatigue, a small number suffer from chronic fatigue syndrome (CFS). CFS is a poorly understood condition characterized by debilitating fatigue and associated symptoms lasting at least six months. Studies indicate that the illness is not simply a manifestation of an underlying psychiatric disorder, but rather is an illness characterized by activation of the immune system, various abnormalities of several hypothalamic-pituitary axes, and reactivation of certain infectious agents.
Korszun A, Papadopoulos E, Demitrack M, Engleberg C, Crofford L.	Department of Psychiatry and School of Dentistry, University of Michigan, Ann Arbor 48109-0840, USA.	The relationship between temporomandibular disorders and stress-associated syndromes.	Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998 Oct;86(4):416-20	OBJECTIVES: The purpose of this study was to determine the comorbidity of temporomandibular disorders and other stress-associated conditions in patients with chronic fatigue syndrome and fibromyalgia. STUDY DESIGN: Of 92 patients who fulfilled the criteria for chronic fatigue syndrome or fibromyalgia (or both), 39 (42%) reported a prior diagnosis of temporomandibular disorder. Further questionnaires were sent to the members of this group, and 30 patients responded. RESULTS: Of the original 92 patients, of whom 42% reported temporomandibular disorders, 46% had histories of irritable bowel syndrome, 42% of premenstrual syndrome, and 19% of interstitial cystitis. Of the patients with temporomandibular disorders, the great majority reported an onset of generalized symptoms before the onset of facial pain. Despite this, 75% had been treated exclusively for temporomandibular disorders, usually with bite splints. CONCLUSIONS: Patients appearing for treatment with chronic facial pain show a high comorbidity with other stress-associated syndromes. The clinical overlap between these conditions may reflect a shared underlying pathophysiologic basis involving dysregulation of the hypothalamic-pituitary-adrenal stress hormone axis in predisposed individuals. A multidisciplinary clinical approach to temporomandibular disorders would improve diagnosis and treatment outcomes for this group of patients.
Kuratsune H, Yamaguti K, Lindh G, Evengard B, Takahashi M, Machii T, Matsumura K, Takaishi J, Kawata S, Langstrom B.	Hematology and Oncology, Osaka University Medical School, Suita, Osaka 565, Japan.	Low levels of serum acylcarnitine in chronic fatigue syndrome and chronic hepatitis type C, but not seen in other diseases.	Int J Mol Med 1998 Jul;2(1):51-6	Recently, we found a serum acylcarnitine (ACR) deficiency in Japanese patients with chronic fatigue syndrome (CFS). To clarify whether this ACR abnormality is a characteristic of CFS or not, we also studied the levels of serum carnitine in Swedish subjects. Both serum ACR and free carnitine (FCR) levels in normal healthy subjects were quite different between Japanese (n=131) and Swedish people (n=46) (p<0.001). However, it is confirmed that Swedish patients with CFS (n=57) also had serum ACR

Kanakura Y, Kitani T, Watanabe Y.				deficiency ($p < 0.001$). When we studied the levels of serum ACR and FCR in Japanese patients with various kinds of diseases (CFS, hematological malignancies, chronic pancreatitis, hypertension, diabetes mellitus, chronic hepatitis type C, psychiatric diseases), a significant decrease in the levels of serum ACR was only found in patients with CFS and chronic hepatitis type C ($p < 0.001$). Therefore, we concluded that ACR deficiency in serum might be a characteristic abnormality in only certain types of diseases.
Kuratsune H, Yamaguti K, Sawada M, Kodate S, Machii T, Kanakura Y, Kitani T.	Department of Hematology and Oncology, Osaka University Medical School, Suita city, Osaka 565, Japan.	Dehydroepiandrosterone sulfate deficiency in chronic fatigue syndrome.	Int J Mol Med 1998 Jan;1(1):143-6	The chronic fatigue syndrome (CFS) is a condition of unknown etiology, characterized by a persistent debilitating fatigue, the muscle-related symptoms and the neuropsychiatric symptoms. Recently, it has been reported that the patients with CFS might have impaired activation of the hypothalamic-pituitary-adrenal axis, and suggested that a part of the patho-genesis of CFS might be associated with abnormalities of the endocrine system. Herein, we show that the majority of Japanese patients with CFS had a serum dehydroepiandrosterone sulfate (DHEA-S) deficiency. Serum DHEA-S is one of the most abundantly produced hormones which is secreted from the adrenal glands, and its physiological function is thought to be a precursor of sex steroids. DHEA-S has recently been shown to have physiological properties, such as neurosteroids, which are associated with such psychophysiological phenomena as memory, stress, anxiety, sleep and depression. Therefore, the deficiency of DHEA-S might be related to the neuropsychiatric symptoms in patients with CFS.
LaManca JJ, Sisto SA, DeLuca J, Johnson SK, Lange G, Pareja J, Cook S, Natelson BH.	Chronic Fatigue Syndrome Cooperative Research Center, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, USA.	Influence of exhaustive treadmill exercise on cognitive functioning in chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):59S-65S	The purpose of this study was to determine the effect of exhaustive exercise on cognitive performance of patients with chronic fatigue syndrome (CFS) and sedentary healthy controls (CON). Subjects were 19 women with CFS and 20 CON. A test battery consisting of 4 cognitive tests (CTB) was given pre-, immediately post-, and 24 hours post-treadmill exercise to exhaustion. No differences were seen on the CTB pre-exercise. CFS patients improved at a slower rate than CON on the Symbol Digit Modalities Test (SDMT), Stroop Word Test (SWT), and Stroop Color Test (SCT). When compared with CON, a lower number of correct responses was seen for the CFS immediately postexercise on the SDMT (61.3 vs 66.2), SWT (137.6 vs 146.6), and SCT (99.4 vs 107.3), and 24 hours postexercise on the SDMT (64.3 vs 69.2), SWT (134.7 vs 148.5), and SCT (101.4 vs 106.3). We conclude that after physically demanding exercise, CFS subjects demonstrated impaired cognitive processing compared with healthy individuals.
Lane RJ, Barrett MC, Taylor DJ, Kemp GJ, Lodi R.	Division of Clinical Neuroscience and Psychological Medicine, Imperial College School of Medicine, Charing Cross Hospital, London, UK. r.lane@cxwms.ac.uk	Heterogeneity in chronic fatigue syndrome: evidence from magnetic resonance spectroscopy of muscle.	Neuromuscul Disord 1998 May;8(3-4):204-9	It has been shown previously that some patients with chronic fatigue syndrome show an abnormal increase in plasma lactate following a short period of moderate exercise, in the sub-anaerobic threshold exercise test (SATET). This cannot be explained satisfactorily by the effects of 'inactivity' or 'deconditioning', and patients with abnormal lactate responses to exercise (SATET) have been found to have significantly fewer Type 1 muscle fibres in quadriceps biopsies than SATET -ve patients. We performed phosphorus magnetic resonance spectroscopy on forearm muscles of 10 SATET patients, 9 SATET -ve patients and 13 sedentary volunteers. There were no differences in resting spectra between these groups but at the end of exercise, intracellular pH in the SATET patients was significantly lower than in both the SATET -ve cases and controls ($P < 0.03$), and the SATET patients also showed a significantly lower ATP synthesis rate during recovery ($P < 0.01$), indicating impaired mitochondrial oxidative phosphorylation. These observations support other evidence which indicates that chronic fatigue syndrome is a heterogeneous disorder, and confirms the view that some chronic fatigue syndrome patients have a peripheral component to their fatigue.
Lane RJ, Barrett MC, Woodrow D, Moss J, Fletcher R, Archard LC.	Division of Neuroscience and Psychological Medicine, Imperial College School of Medicine, Charing Cross Hospital, London, UK. r.lane@cxwms.ac.uk	Muscle fibre characteristics and lactate responses to exercise in chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1998 Mar;64(3):362-7	OBJECTIVES: To examine the proportions of type 1 and type 2 muscle fibres and the degree of muscle fibre atrophy and hypertrophy in patients with chronic fatigue syndrome in relation to lactate responses to exercise, and to determine to what extent any abnormalities found might be due to inactivity. METHODS: Quadriceps needle muscle biopsies were obtained from 105 patients with chronic fatigue syndrome and the proportions of type 1 and 2 fibres and fibre atrophy and hypertrophy factors were determined from histochemical preparations, using a semiautomated image analysis system. Forty one randomly selected biopsies were also examined by electron microscopy. Lactate responses to exercise were measured in the subanaerobic threshold exercise test (SATET). RESULTS: Inactivity would be expected to result in a shift to type 2 fibre predominance and fibre atrophy, but type 1 predominance (23%) was more common than type 2 predominance (3%), and fibre atrophy was found in only 10.4% of cases. Patients with increased lactate responses to exercise did have significantly fewer type 1 muscle fibres ($p < 0.043$ males, $p < 0.0003$ females), but there was no evidence that this group was less active than the patients with normal lactate responses. No significant ultrastructural abnormalities were found. CONCLUSION: Muscle histometry in

				patients with chronic fatigue syndrome generally did not show the changes expected as a result of inactivity. However, patients with abnormal lactate responses to exercise had a significantly lower proportion of mitochondria rich type 1 muscle fibres.
Lange G, Wang S, DeLuca J, Natelson BH.	Department of Psychiatry, Chronic Fatigue Syndrome Center, University of Medicine and Dentistry-New Jersey Medical School, Newark, USA.	Neuroimaging in chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):50S-53S	The diagnosis of chronic fatigue syndrome (CFS) is made difficult by the absence of specific biomedical markers, and depends primarily on determining whether subjective information provided by the patient meets the clinical case definition of this syndrome. Reported cognitive difficulties and/or complaints of headache may instigate referral for brain imaging. This article will discuss the value of neuroimaging in evaluating CFS, specifically reviewing studies that (1) used static magnetic resonance imaging (MRI) to assess structural abnormalities; and (2) assessed regional cerebral blood flow (rCBF) via detection of Tc-99m hexamethylpropyl-eneamine oxime distribution by single-photon emission computed tomography (SPECT). Future research design considerations are explored including (1) the utilization of positron emission tomography (PET) and other emerging neuroimaging technologies; and (2) methodological concerns, i.e., the influence of psychopathology (such as depression) and neurologic disease (such as multiple sclerosis) as possible confounding factors.
Lavietes MH, Michael T. Bergen, Benjamin H. Natelson		Measurement of CO ₂ in Chronic Fatigue Syndrome Patients	Journal of Chronic Fatigue Syndrome 1998: 4(3): 3 - 11	This study has two goals: one, to compare the resting end-tidal pCO ₂ (PetCO ₂) and heart rate (HR) of chronic fatigue syndrome patients (CFS) with controls; two, to examine the effects of a mouthpiece and noseclips upon measurements of PetCO ₂ and HR. Patients from the CFS Center came to the University Hospital pulmonary function laboratory for one testing session. Arterial (PaCO ₂), PetCO ₂ , end-nasal (PenCO ₂) and HR were measured twice; both with and again without the subject breathing through the mouthpiece. We found that PenCO ₂ was greater and HR lower for both CFS and non-CFS groups when subjects were not confined by the mouthpiece. We conclude that there is no abnormality in the regulation of respiration in CFS patients. Changes in HR accompany changes in PetCO ₂ in this study. Most likely, both result from anxiety associated with mouthpiece breathing
Laylander JA		A Nutrient/Toxin Interaction Theory of the Etiology and Pathogenesis of Chronic Pain-Fatigue Syndromes: Part II	Journal of Chronic Fatigue Syndrome 1998: 5(1): 93 - 126	This second part of the review paper covers the evidence in favor of the theory which proposes that Chronic Fatigue Syndrome, Fibromyalgia Syndrome, and Persian Gulf Syndrome represent finitely variable combinations of multiple systemic dysfunctions which share a common underlying etiology at the subcellular level: magnesium deficiency plus concomitant fluoride excess (MDFE). Treatment suggestions are listed at the end of the manuscript through a call for clinical trials to test the theory presented
Laylander JA		A Nutrient/Toxin Interaction Theory of the Etiology and Pathogenesis of Chronic Pain-Fatigue Syndromes: Part I	Journal of Chronic Fatigue Syndrome 1998: 5(1): 67 - 91	Recent research suggests that Chronic Fatigue Syndrome (CFS), Fibromyalgia Syndrome (FMS), and Persian Gulf Syndrome (PGS) may represent the effects of dysfunctions involving the central and/or peripheral nervous system, neuroendocrine system, neuromuscular system, immune system, metabolism, or sleep patterns. Each systemic dysfunction is accepted here as being central to these syndromes but not causal. This two-part review introduces the theory that the syndromes listed above represent finitely variable combinations of multiple systemic dysfunctions which all share a common underlying etiology at the subcellular level: magnesium deficiency plus concomitant fluoride excess (MDFE). The theory is introduced in Part I; detailed evidence which supports the theory is presented in Part II. Treatment suggestions are listed at the end of Part II through a call for clinical trials to test this theory.
Layzer RB.		Asthenia and the chronic fatigue syndrome.	Muscle Nerve 1998 Dec;21(12):1609-11	
Lee P.	Institute of Health Policy Studies, University of California, San Francisco, 94109, USA.	Recent developments in chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):1S	
Levine PH, Fears TR, Cummings P, Hoover RN.	Division of Cancer Epidemiology and Genetics, NIH, Bethesda, Maryland 20892, USA.	Cancer and a fatiguing illness in Northern Nevada--a causal hypothesis.	Ann Epidemiol 1998 May;8(4):245-9	PURPOSE: We investigated the possibility that chronic fatigue syndrome (CFS) predisposes to cancer by comparing the cancer pattern in an area in northern Nevada, where an outbreak of a fatiguing illness, which included cases of CFS, was reported, to an area in southern Nevada, where no such illness was reported. METHODS: Data from the computerized Nevada Cancer Registry were utilized to compare incidence rates of four malignancies--brain cancer, non-Hodgkin lymphoma (NHL), lung cancer, and breast cancer--in Washoe and Lyon Counties, where an unexplained fatiguing illness was reported during 1984-86, with comparably sized Clark County, where no such illness was reported. RESULTS: Higher incidences of NHL and primary brain tumors were noted in the two northern Nevada counties (Washoe and Lyon) in 1986 and 1987 respectively, compared to the southern Nevada (Clark) county. Similar patterns were not seen for

				breast or lung cancer. CONCLUSIONS: This study provides a model for investigating the possible predisposition of CFS patients to develop cancer using other cohorts, but it is currently premature to accept such a link at this time.
Levine PH, Whiteside TL, Friberg D, Bryant J, Colclough G, Herberman RB.	National Cancer Institute, Bethesda, Maryland, 20892, USA.	Dysfunction of natural killer activity in a family with chronic fatigue syndrome.	Clin Immunol Immunopathol 1998 Jul;88(1):96-104	A family was identified with 5 of 6 siblings and 3 other immediate family members who had developed chronic fatigue syndrome (CFS) as adults. All 8 met criteria for the CFS case definition as recommended by the Centers for Disease Control and Prevention. Sixty-eight blood samples were obtained over a period of 2 years from 20 family members (8 affected, 12 unaffected) and 8 normal controls. All blood samples were tested for NK activity in 4-h ⁵¹ Cr-release assays and for the number of circulating CD3-CD56(+) and CD3-CD16(+) by flow cytometry. NK activity of the affected immediate family members (cases, n = 8) was significantly lower (P = 0.006, two-sided) than that of the concurrently tested normal controls. The results for unaffected family members were intermediate between these two groups, and the pairwise comparison of unaffected family members to either cases or controls showed no statistically significant difference (P = 0.29, two-sided). No differences were seen between the groups in the absolute number of CD3-CD56(+) or CD3-CD16(+) lymphocytes in the peripheral blood. Familial CFS was associated with persistently low NK activity, which was documented in 6/8 cases and in 4/12 unaffected family members. In the family with 5 of 6 siblings who had documented CFS, 2 of their offspring had pediatric malignancies. Low NK activity in this family may be a result of a genetically determined immunologic abnormality predisposing to CFS and cancer.
Levine PH.	Viral Epidemiology Branch, National Cancer Institute, Bethesda, Maryland, USA.	Chronic fatigue syndrome comes of age.	Am J Med 1998 Sep 28;105(3A):2S-6S	
Levine PH.	George Washington University Medical Center, Washington, DC, USA.	What we know about chronic fatigue syndrome and its relevance to the practicing physician.	Am J Med 1998 Sep 28;105(3A):100S-103S	A number of recent reports have emphasized laboratory abnormalities, clinical tests, and therapeutic approaches that appear to have great promise in the evaluation and management of chronic fatigue syndrome (CFS). Because of the heterogeneity of CFS, the cost of many of these assays and procedures, and the frequent lack of skilled consultants able to apply relevant sophisticated procedures, the solo healthcare provider is often left with uncertain options in patient management. This article summarizes current approaches to patient management, utilizing available information relevant to CFS.
Litzman J, Lokaj J, Fucikova T.	Ustav klinické imunologie a alergologie, FN u sväte Anny, Brno, Praha.	[Chronic fatigue syndrome].[article in Czech]	Cas Lek Cesk 1998 May 18;137(10):295-8	A great concern is recently given to the chronic fatigue syndrome in the Czech Republic. Unfortunately, published data allow us to state neither the etiologic agent nor the pathophysiology of the disease. Although many authors published various laboratory abnormalities, these changes are inconstant and do not allow to state a diagnosis of the chronic fatigue syndrome by a single laboratory test, and effective therapy is not known either. Psychotherapy, and in some cases antidepressants, are recommended by some authors to alleviate patient's symptoms. Neither immunological nor antiviral therapy showed positive results in controlled trials and are not generally used in most centers.
Lloyd AR.	The Inflammation Research Unit, School of Pathology, University of New South Wales, Sydney, Australia.	Chronic fatigue and chronic fatigue syndrome: shifting boundaries and attributions.	Am J Med 1998 Sep 28;105(3A):7S-10S	The subjective symptom of "fatigue" is one of the most widespread in the general population and is a major source of healthcare utilization. Prolonged fatigue is often associated with neuropsychological and musculoskeletal symptoms that form the basis of several syndromal diagnoses including chronic fatigue syndrome, fibromyalgia, and neurasthenia, and is clearly not simply the result of a lack of force generation from the muscle. Current epidemiologic research in this area relies predominantly on self-report data to document the prevalence and associations of chronic fatigue. Of necessity, this subjective data source gives rise to uncertain diagnostic boundaries and consequent divergent epidemiologic, clinical, and pathophysiologic research findings. This review will highlight the impact of the case definition and ascertainment methods on the varying prevalence estimates of chronic fatigue syndrome and patterns of reported psychological comorbidity. It will also evaluate the evidence for a true postinfective fatigue syndrome.
Loblay RH.		Chronic fatigue syndrome.	Lancet 1998 Apr 25;351(9111):1292 Comment on: Lancet. 1998 Feb 21;351(9102):574	
Low PA.	Mayo Medical School, Department of Neurology, Mayo Clinic, Rochester, MN	Autonomic neuropathies.	Curr Opin Neurol 1998 Oct;11(5):531-7	A limited autonomic neuropathy may underlie some unusual clinical syndromes, including the postural tachycardia syndrome, pseudo-obstruction syndrome, heat intolerance, and perhaps chronic fatigue syndrome. Antibodies to autonomic structures are common in diabetes, but their specificity is unknown.

	55905, USA.			The presence of autonomic failure worsens prognosis in the diabetic state. Some autonomic neuropathies are treatable. Familial amyloid polyneuropathy may respond to liver transplantation. There are anecdotal reports of acute panautonomic neuropathy responding to intravenous gamma globulin. Orthostatic hypotension may respond to erythropoietin or midodrine.
Lynch S, Fraser J.		Fluoxetine and graded exercise in chronic fatigue syndrome.	Br J Psychiatry 1998 Oct;173:353 Comment on: Br J Psychiatry. 1998 Jun;172:485-90	
MacHale SM, Cavanagh JT, Bennie J, Carroll S, Goodwin GM, Lawrie SM.	Department of Psychiatry, University of Edinburgh, Edinburgh, UK.	Diurnal variation of adrenocortical activity in chronic fatigue syndrome.	Neuropsychobiology 1998 Nov;38(4):213-7	Baseline morning and evening serum cortisol and ACTH concentrations, and diurnal changes in hormone levels, were measured in 30 patients with chronic fatigue syndrome (CFS) but without concurrent depressive disorder and a control group of 15 weight-, age- and sex-matched healthy volunteers. Morning cortisol levels were non-significantly lower in CFS patients, while evening levels were non-significantly higher. ACTH concentrations were non-significantly higher in both the morning and evening. The diurnal change in cortisol levels was significantly less in CFS than in controls ($p < 0.05$). In CFS subjects, evening levels of cortisol correlated significantly with measures of general health and physical functioning, while diurnal change in cortisol was positively correlated with measures of functional improvement over the past year and current social functioning. These results suggest that there is a relationship between adrenocortical function and disability in CFS, but do not reveal the causal connection.
Mackinnon LT.	Department of Human Movement Studies, The University of Queensland, Australia.	Future directions in exercise and immunology: regulation and integration.	Int J Sports Med 1998 Jul;19 Suppl 3:S205-9; discussion S209-11	Although it is difficult to predict future directions in a rapidly expanding field such as exercise immunology, recently published research along with that presented at this Symposium allow us to ask some key questions which may point to new directions: 1) Are athletes immunocompromised? Athletes are not clinically immunodeficient, yet endurance athletes are at increased risk of illness. Long-term prospective studies are needed to understand the relationship between infection, training variables and immune parameters. 2) Is downregulation of nonspecific immunity beneficial or harmful? In athletes, neutrophils appear to be downregulated, and this may alter resistance to illness. Alternatively, neutrophils are mediators of tissue damage during inflammation. Downregulation of neutrophil function may be protective by limiting chronic inflammation. In athletes, mild immunosuppression may reflect a compromise between the body's attempts to limit inflammation while maintaining immune function. 3) What mediates communication between events in skeletal muscle and the immune system? Leukocyte mobility is affected by metabolic and mechanical factors during exercise. Exercise increases cytokine levels in damaged skeletal muscle and expression of adhesion molecules. Future work is likely to focus on the role of cytokines and adhesion molecules in mediating exercise-induced changes in leukocyte mobility. 4) Can exercise training provide a "countermeasure" against immunosuppressive events? Moderate exercise training may have a role in stimulating the immune system during certain diseases (e.g., HIV-infection), immune dysfunction (e.g., chronic fatigue syndrome) or reduced responsiveness (e.g. aging, spaceflight). It is also likely that future study will apply molecular biology techniques to further identify mechanisms by which exercise influences immune function.
Marlin RG, Anchel H, Gibson JC, Goldberg WM, Swinton M.	MRS Health Services, St. Joseph's Hospital, and McMaster University, Hamilton, Ontario, Canada.	An evaluation of multidisciplinary intervention for chronic fatigue syndrome with long-term follow-up, and a comparison with untreated controls.	Am J Med 1998 Sep 28;105(3A):110S-114S	Individuals meeting the Fukuda et al definition for chronic fatigue syndrome completed a multidisciplinary assessment that included medical, psychiatric, behavioral, and psychological evaluations. Patients were then offered a comprehensive multidisciplinary intervention that included (1) bringing the patient under optimal medical management; (2) treating any ongoing affective or anxiety disorder pharmacologically; and (3) implementing a comprehensive cognitive-behavioral treatment program. Fifty-one patients proceeded to treatment. The cognitive-behavioral component was carried out through the use of a therapist working with the patients in their own environments. The program was individually tailored to patients, but included (1) structured physical exercise and activation; (2) sleep management strategies; (3) careful activity management; (4) regulation of stimulant intake and reductions in use of symptomatic medications; (5) cognitive intervention designed to deal with patients' beliefs concerning the nature of their disorder; (6) participation of patients' family; and (7) efforts to establish specific vocational and avocational goals. Third parties were encouraged to collaborate cooperatively. Employers were urged to provide employment opportunities and facilitate a graduated but time-targeted return to work. Disability carriers were encouraged to provide interim financial support in the form of disability benefits, support therapeutic intervention, but also to establish a clear time-frame to access to benefits. Of 51 treated patients, 31

				returned to gainful employment, 14 were functioning at a level equivalent to employment, and 6 remained significantly disabled. Twenty of the original 71 patients were contacted an average of 33 months later. Patients who had been treated showed good maintenance of gains. Untreated patients showed improvement in only a minority of cases.
Martin WJ.	Center for Complex Infectious Diseases, Rosemead, Calif 91770, USA.	Cellular sequences in stealth viruses.	Pathobiology 1998;66(2):53-8	Cloned DNA obtained from the culture of an African green monkey simian cytomegalovirus-derived stealth virus contains multiple discrete regions of significant sequence homology (p values ranging from 4×10^{-3} to 1×10^{-20}) to portions of known human cellular genes. The stealth virus was cultured from a patient with chronic fatigue syndrome (CFS). Earlier studies had revealed considerable sequence heterogeneity within DNA fragments isolated from virus-infected cells. A set of polymerase chain reaction (PCR) primers generated different PCR products when tested on stealth virus cultures from 4 patients with CFS. Several of the PCR products also contain regions of significant partial homology to distinct cellular sequences, including sequences repetitively expressed throughout the cellular genome. Stealth viruses may play an important role in the origins and in the genetic diversity of both viral and cellular sequences.
McCluskey DR.	Queens University of Belfast, Ireland.	Chronic fatigue syndrome: Its cause and a strategy for management.	Compr Ther 1998 Aug;24(8):357-63	This article describes the features of chronic fatigue syndrome and, by analysis of the many clinical paradoxes which it manifests, attempts to give a unifying explanation of the cause of the disorder and a strategy for management.
McKenzie R, O'Fallon A, Dale J, Demitrack M, Sharma G, Deloria M, Garcia-Borreguero D, Blackwelder W, Straus SE.	Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892-1888, USA.	Low-dose hydrocortisone for treatment of chronic fatigue syndrome: a randomized controlled trial.	JAMA 1998 Sep 23-30;280(12):1061-6 Comment in: JAMA. 1999 May 26;281(20):1887-8; discussion 1888-9 JAMA. 1999 May 26;281(20):1887; discussion 1888-9 JAMA. 1999 May 26;281(20):1888-9	CONTEXT: Chronic fatigue syndrome (CFS) is associated with a dysregulated hypothalamic-pituitary-adrenal axis and hypocortisolemia. OBJECTIVE: To evaluate the efficacy and safety of low-dose oral hydrocortisone as a treatment for CFS. DESIGN: A randomized, placebo-controlled, double-blind therapeutic trial, conducted between 1992 and 1996. SETTING: A single-center study in a tertiary care research institution. PATIENTS: A total of 56 women and 14 men aged 18 to 55 years who met the 1988 Centers for Disease Control and Prevention case criteria for CFS and who withheld concomitant treatment with other medications. INTERVENTION: Oral hydrocortisone, 13 mg/m ² of body surface area every morning and 3 mg/m ² every afternoon, or placebo, for approximately 12 weeks. MAIN OUTCOME MEASURES: A global Wellness scale and other self-rating instruments were completed repeatedly before and during treatment. Resting and cosyntropin-stimulated cortisol levels were obtained before and at the end of treatment. Patients recorded adverse effects on a checklist. RESULTS: The number of patients showing improvement on the Wellness scale was 19 (54.3%) of 35 placebo recipients vs 20 (66.7%) of 30 hydrocortisone recipients (P = .31). Hydrocortisone recipients had a greater improvement in mean Wellness score (6.3 vs 1.7 points; P = .06), a greater percentage (53% vs 29%; P = .04) recording an improvement of 5 or more points in Wellness score, and a higher average improvement in Wellness score on more days than did placebo recipients (P < .001). Statistical evidence of improvement was not seen with other self-rating scales. Although adverse symptoms reported by patients taking hydrocortisone were mild, suppression of adrenal glucocorticoid responsiveness was documented in 12 patients who received it vs none in the placebo group (P < .001). CONCLUSIONS: Although hydrocortisone treatment was associated with some improvement in symptoms of CFS, the degree of adrenal suppression precludes its practical use for CFS.
Meyer FP.		ber die laquo;Omnipotenz>> der Chelattherapie.	Forsch Komplementarmed 1998;5(6):266-271	About the 'Omnipotence' of the Chelation Therapy In the eighties the 'method of treatment proven in many thousands of cases over 20 years' was transferred from the USA to Germany (enjoys a priori considerable faith) using very dubious promises. It was Clarke et al. who introduced this 'therapy' in 1955. The dubious promise was to maintain that the chelation therapy eliminates or alleviates symptoms in the case of the following illnesses: Alzheimer's disease, senility, schizophrenia, rheumatoid arthritis, osteoarthritis, gout, renal calculus, apoplectic coma, gallstones, multiple sclerosis, osteoporosis, chronic fatigue syndrome, varicose veins, hypertension, failure of memory, scleroderma, Raynaud's disease, digitalis intoxication, intermittent claudication, diabetic ulcer, disturbance of the blood supply, ulcer on the legs, snake poison, impotence, emotional difficulties, defective hearing, vision disorder. There is not the slightest proof of effectiveness for any of the listed indications. The burden of proof lies with the supplier. Even in the case of the relatively often examined peripheral atherosclerotic changes (claudicatio intermittens) there is no proof that EDTA has a greater effect than placebo. For coronary heart disease too there is no evidence for any usefulness of the chelation therapy beyond that of a placebo effect. Only controlled studies can help to improve the therapy in the sense of 'Evidence-based medicine'. Retrospective investigations on thousands of patients cannot 'prove' anything, although this is maintained again and again.
Michiels V, Cluydts R,	Department of Psychology,	Attention and verbal learning	J Int Neuropsychol Soc 1998	Former neuropsychological studies with Chronic Fatigue Syndrome (CFS) patients evaluated a broad range

Fischler B.	Free University of Brussels, Belgium. vmichiel@vub.ac.be	in patients with chronic fatigue syndrome.	Sep;4(5):456-66	of cognitive functions. Several, but not all, reported subtle attentional and memory impairments suggesting possible mild cerebral involvement. In this study, a battery of attentional tests and a verbal memory task were administered to 20 CFS patients and 22 healthy controls (HC) in order to clarify the specific nature of attention and memory impairment in these patients. The results provide evidence for attentional dysfunction in patients with CFS as compared to HC. CFS patients performed more poorly on a span test measuring attentional capacity and working memory. Speeded attentional tasks with a more complex element of memory scanning and divided attention seem to be a sensitive measure of reduced attentional capacity in these patients. Focused attention, defined as the ability to attend to a single stimulus while ignoring irrelevant stimuli, appears not to be impaired. CFS patients were poorer on recall of verbal information across learning trials, and poor performance on delayed recall may be due to poor initial learning and not only to a retrieval failure.
Miller BJ, John L. Whiting, Andrew D. Clouston		Coincidental Splenectomy in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998; 4(1): 37 - 42	A unique case of coincidental splenectomy for trauma during chronic fatigue syndrome (CFS) is presented. The patient had a two-year history of CFS prior to her involvement in a road crash. Delayed rupture of the spleen ten days later necessitated urgent laparotomy. At operation, the splenic parenchyma was spongy and friable. Splenorrhaphy was considered inadvisable and a splenectomy was performed. Histological examination of the spleen revealed chronic inflammatory changes of uncertain etiology. One year post-operatively, the patient recovered from her CFS symptoms and returned to work. These histopathological changes in the spleen of a patient with CFS have not been described before.
Moorkens G, Wynants H, Abs R.	Department of Internal Medicine, University Hospital Antwerp, Belgium.	Effect of growth hormone treatment in patients with chronic fatigue syndrome: a preliminary study.	Growth Horm IGF Res 1998 Apr;8 Suppl B:131-3	The efficacy of growth hormone (GH) therapy was evaluated in patients with chronic fatigue syndrome (CFS) who had peak serum GH levels below 10 microg/l during stage-controlled sleep. Twenty patients (7 men, 13 women; age range, 30-60 years) with CFS were randomized to receive placebo or GH therapy, 6.7 microg/kg/day (0.02 IU/kg/day), for 12 weeks. Following this double-blind treatment period, the 17 patients remaining in the study were given GH therapy at the above dose for an open period of 9 months. Mean (SD) serum levels of insulin-like growth factor I (IGF-I) increased during GH treatment, from 173.46 microg/l to 296.89 microg/l ($P < 0.001$); IGF-I SDS values increased from -0.45 to 0.43 ($P < 0.001$). Fat-free mass and total body water were significantly increased after 12 months of treatment. Although quality of life, as assessed using two different questionnaires, did not improve significantly during GH treatment, four patients were able to resume work after a long period of sick leave.
Morehouse RL, Flanigan M, MacDonald DD, Braha D, Shapiro C.	Department of Psychiatry, Dalhousie University, QEII Health Sciences Centre, Halifax, Nova Scotia.	Depression and short REM latency in subjects with chronic fatigue syndrome.	Psychosom Med 1998 May-Jun;60(3):347-51	OBJECTIVE: The hypothesized polysomnographic marker for depression, Rapid Eye Movement Latency (REML), was used to investigate two groups of subjects; Chronic Fatigue Syndrome (CFS)-not depressed and CFS-depressed. METHOD: CFS subjects were classified into depressed and not depressed groups, using the Diagnostic Interview Schedule (DIS), and subsequently were studied in a sleep laboratory to ascertain REML. RESULTS: Short REML showed a statistically significant correlation with the depressed state in CFS subjects. CONCLUSION: Short REM latency is associated with depression in the CFS population.
Morriss RK, Wearden AJ, Mullis R.	Department of Community Psychiatry, University of Manchester, UK.	Exploring the validity of the Chalder Fatigue scale in chronic fatigue syndrome.	J Psychosom Res 1998 Nov;45(5):411-7	The Chalder fatigue scale is widely used to measure physical and mental fatigue in chronic fatigue syndrome patients, but the constructs of the scale have not been examined in this patient sample. We examined the constructs of the 14-item fatigue scale in a sample of 136 chronic fatigue syndrome patients through principal components analysis, followed by correlations with measures of subjective and objective cognitive performance, physiological measures of strength and functional work capacity, depression, anxiety, and subjective sleep difficulties. There were four factors of fatigue explaining 67% of the total variance. Factor 1 was correlated with subjective everyday cognitive difficulties, concentration difficulties, and a deficit in paired associate learning. Factor 2 was correlated with difficulties in maintaining sleep. Factor 3 was inversely correlated with grip strength, peak VO ₂ , peak heart rate, and peak functional work capacity. Factor 4 was correlated with interview and self-rated measures of depression. The results support the validity of mental and physical fatigue subscales and the dropping of the "loss of interest" item in the 11-item version of the fatigue scale.
Morriss RK, Wearden AJ.	Department of Psychiatry, University of Manchester, UK.	Screening instruments for psychiatric morbidity in chronic fatigue syndrome.	J R Soc Med 1998 Jul;91(7):365-8	Physicians require a screening instrument to detect psychiatric disorders in patients with chronic fatigue syndrome (CFS). Different threshold scores on the Hospital Anxiety and Depression scale (HAD) and the mental health scale of the Medical Outcome Survey (MOS) were compared with two gold standards for the presence or absence of psychiatric disorder, standard diagnostic criteria (DSM-III-R) and a threshold score for the number of psychiatric symptoms at a standardized psychiatric interview (Revised Clinical Interview

				Schedule total cut-off score of 11/12). They were compared by use of validating coefficients and receiver operating characteristics in 136 consecutive CFS medical outpatients. The HAD scale at cut-off of 9/10 was a valid and efficient screening instrument for anxiety and depression by comparison with both gold standards. The MOS mental health scale at its recommended cut-off score of 67/68 yielded too many false-positives to be recommended as a psychiatric screening instrument in CFS patients.
Natelson BH, Cheu J, Hill N, Bergen M, Korn L, Denny T, Dahl K.	Department of Neurosciences, University of Medicine and Dentistry of New Jersey, Newark, USA. bhn@nbunj.jvnc.net	Single-blind, placebo phase-in trial of two escalating doses of selegiline in the chronic fatigue syndrome.	Neuropsychobiology 1998;37(3):150-4	AIM: To perform a clinical trial of selegiline in 25 patients with chronic fatigue syndrome (CFS) where patients were told they would receive placebo or active agent at different times during the 6-week trial. We chose selegiline, a specific monoamine oxidase (MAO) B receptor inhibitor, because a prior trial of lowdose phenelzine, a nonspecific MAO inhibitor, showed a small but significant therapeutic effect. METHODS: Questionnaires comprised of 19 tests of mood, fatigue, functional status and symptom severity were collected at the start and end of the trial as well as 2 weeks after its start. The trial was done in three 2-week blocks: in the first, 2 placebo pills were given per day; in the next, one 5-mg tablet of agent and one placebo were given per day, and in the last, a 5-mg tablet of agent was given twice a day. The plan was to compare the changes in the 19 tests during the placebo phase to those found in the active treatment phase in 19 patients completing the trial. FINDINGS: Significant improvement in 3 variables-tension/anxiety, vigor and sexual relations-was found. A significant pattern of improvement compared to worsening was found for the 19 self-report vehicles during active treatment as compared with placebo treatment. Evidence for an antidepressant effect of the drug was not found. CONCLUSIONS: Selegiline has a small but significant therapeutic effect in CFS which appears independent of an antidepressant effect.
Natelson BH, LaManca JJ, Denny TN, Vladutiu A, Oleske J, Hill N, Bergen MT, Korn L, Hay J.	Department of Neurosciences, Chronic Fatigue Syndrome Cooperative Research Center, University of Medicine and Dentistry of New Jersey--New Jersey Medical School, Newark 07018, USA.	Immunologic parameters in chronic fatigue syndrome, major depression, and multiple sclerosis.	Am J Med 1998 Sep 28;105(3A):43S-49S	The purpose of this study was to evaluate the immune dysfunction hypothesis of chronic fatigue syndrome (CFS) by comparing immunologic data from patients with CFS with data from patients with other fatiguing illnesses--major depression and multiple sclerosis (MS)--and with data from healthy sedentary controls. The subjects were 65 healthy sedentary controls, 71 CFS patients (41 with no axis-I diagnosis), 23 patients with mild MS, and 21 patients with major depression. Blood was sampled and assayed for the following: (1) immunologic serologic variables--circulating immune complexes (i.e., Raji cell and C1q binding), immunoglobulins A, E, G, and M, and IgG subclasses; (2) cell surface activation markers--the proportion of CD4 cells expressing CD45RA and CD45RO and the proportion of CD8 cells expressing CD38, CD11b-, HLA-DR and CD28; and (3) natural killer (NK) total cell count as well as the proportion of lymphocytes expressing NK cell surface markers (i.e., CD3-/CD16 and CD56. Of the 18 variables studied, differences between CFS patients and controls were found only for IgG1 and IgG3. When CFS patients were stratified by the presence or absence of concurrent axis-I disease, it was the group with axis-I disorder that had the lowest IgG1 values--contrary to expectation. When data from patients with MS and major depression were also evaluated, the subclass deficiency was no longer significant. The one group to show evidence for immune activation (i.e., an elevated proportion of CD4 cells expressing the CD45RA activation marker) was the group with mild MS. These data support neither immune dysfunction nor immune activation in CFS or in major depression, for the variables studied. The reductions in IgG subclasses may be an epiphenomenon of patient or control subject composition. In contrast, MS, even in the mild and early stages, as in the patients studied here, is associated with immune activation.
Newman ME, Shapira B, Lerer B.	Biological Psychiatry Laboratory, Dept. of Psychiatry, Hadassah - Hebrew University Medical Center.	Evaluation of central serotonergic function in affective and related disorders by the fenfluramine challenge test: a critical review.	Int J Neuropsychopharmacol 1998 Jul;1(1):49-69	Plasma prolactin levels following oral administration of the serotonin (5-HT) releasing agent, fenfluramine hydrochloride, have been extensively used to evaluate central serotonergic function in affective and related disorders. Cortisol responses to fenfluramine have generally been a less informative measure. In healthy subjects, prolactin release by fenfluramine is dose-dependent, blocked by antagonists of serotonin receptors of the 5-HT-2a/2c type, negatively correlated with age and increased in young females. In major depression, a preponderance of studies have found blunted prolactin responses compared to matched normal controls. Although a significant minority of studies have not found blunting, increased prolactin release has not been observed. The blunted prolactin release is not due to a deficient secretory capacity of pituitary lactotrophs and is congruent with other evidence for reduced central serotonergic function in major depression. Blunting of the prolactin response may be associated with severity of depression and with elevated baseline cortisol levels. Treatment with antidepressant drugs and electroconvulsive therapy has been reported to increase the prolactin response but this has not been replicated in all studies. Blunted prolactin responses to fenfluramine have been fairly consistently associated with impulsive aggression in different personality disorders and with severity of suicide attempts in depressed patients. A number of studies employing the

				fenfluramine challenge test (FCT) have been conducted in obsessive compulsive disorder but their results have been variable. Prolactin responses to fenfluramine may be enhanced in panic disorder and chronic fatigue syndrome but the number of studies in these conditions is small as is the case for seasonal affective disorder. Since the therapeutic administration of fenfluramine as an appetite suppressant has been suspended because of reports of cardiac complications, further use of this compound as a challenge agent is not anticipated. Future studies are likely to employ agents acting on specific serotonin receptors and should apply methodological insights from the use of the FCT, which are considered in this review. Use of concomitant brain imaging to evaluate the central effects of challenge agents directly is likely to become more prevalent and may supplant neuroendocrine challenge paradigms such as the FCT which have been remarkably heuristic but are limited in scope and methodologically complex.
Nicolson GL, Nicolson NL.	Institute for Molecular Medicine, Huntington Beach, CA 92649-1041, USA. gnicimm@ix.netcom.com	Gulf War illnesses: complex medical, scientific and political paradox.	Med Confl Surviv 1998 Apr-Jun;14(2):156-65	Gulf War illnesses are a collection of disorders that for the most part can be diagnosed and treated, if effective programmes exist to assist veterans, and in some cases their immediate family members. Although these illnesses are complex and have multi-organ signs and symptoms, a proportion of these patients can be identified as having Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) and/or Fibromyalgia Syndrome (FMS). Although there are many possible causes of CSF/ME/FMS, chronic infections can explain, at least in a subset of patients, the apparent transmission of these illnesses to family members and the appearance of chronic, multi-organ and auto-immune signs and symptoms. Unfortunately, many veterans who have been diagnosed with chronic infections, such as mycoplasmal infections, cannot obtain adequate treatment for their condition, resulting in their reliance on private physicians and clinics for assistance. This lack of response may ultimately be responsible for the transmission of the illness to non-veterans.
Nisenbaum R, Reyes M, Mawle AC, Reeves WC.	Klemm Analysis Group, Atlanta, GA, USA.	Factor analysis of unexplained severe fatigue and interrelated symptoms: overlap with criteria for chronic fatigue syndrome.	Am J Epidemiol 1998 Jul 1;148(1):72-7	The objective of this study was to identify factors explaining the correlations among unexplained severe fatigue of different durations (1-5 months or > or =6 months) and symptoms reported as being significant health problems during a preceding 4-week period. Between June and December of 1994, a cross-sectional, random digit dialing telephone survey was conducted among residents of San Francisco, California. All subjects who reported having severe fatigue lasting for > or =1 month and a random sample of nonfatigued subjects were asked to participate in a detailed telephone interview. Data from 1,510 individuals aged 18-60 years who did not have medical or psychiatric conditions that could explain their severe fatigue were analyzed. Common factor analyses identified three correlated factors (defined as "fatigue-mood-cognition" symptoms, "flu-type" symptoms, and "visual impairment") that explained the correlations among fatigue lasting for > or =6 months and 14 interrelated symptoms. No factor explained the correlations among fatigue lasting for 1-5 months and other symptoms. The combination of fatigue of > or =6 months' duration and selected symptoms overlaps with published criteria used to define cases of chronic fatigue syndrome (CFS). Although symptoms described in this study were reported as appearing within the preceding month, and CFS symptoms must have been present for the previous 6 months, these results provide empirical support for the interrelations among unexplained fatigue of > or =6 months' duration and symptoms included in the CFS case definition.
Ogawa M, Nishiura T, Yoshimura M, Horikawa Y, Yoshida H, Okajima Y, Matsumura I, Ishikawa J, Nakao H, Tomiyama Y, Kanayama Y, Kanakura Y, Matsuzawa Y.	Osaka University Medical School, Osaka, Japan.	Decreased nitric oxide-mediated natural killer cell activation in chronic fatigue syndrome.	Eur J Clin Invest 1998 Nov;28(11):937-43	BACKGROUND: L-Arginine (L-Arg), one of the essential amino acids, has been reported to have an immunomodulatory effect. The precise mechanism of the L-Arg-induced natural killer (NK) cell activation remains unresolved, and the effect of L-Arg on NK cells in chronic fatigue syndrome (CFS) patients has not been estimated. METHODS: NK cell function was evaluated in 20 subjects with CFS and compared with that in 21 healthy individuals. RESULTS: In healthy control subjects, NK activity was significantly increased after treatment with L-Arg, an NK function enhancer, for 24 h, whereas the same treatment failed to enhance NK activity in the CFS patients. We thus focused on L-Arg metabolism, which involves nitric oxide (NO) production through NO synthase (NOS). The expression of inducible NO synthase (iNOS) transcripts in peripheral blood mononuclear cells was not significantly different between healthy control subjects and CFS patients. The L-Arg-mediated NK cell activation was abolished by addition of NG-monomethyl-L-arginine, an inhibitor for iNOS. Furthermore, incubation with S-nitroso-N-acetylpenicillamine, an NO donor, stimulated NK activity in healthy control subjects but not in CFS patients. CONCLUSION: These results demonstrate that the L-Arg-induced activation of NK activity is mediated by NO and that a possible dysfunction exists in the NO-mediated NK cell activation in CFS patients.
Olson LG, Cole MF,	Sleep Disorders Centre,	Correlations among Epworth	J Sleep Res 1998	The aim of this study was to identify factors other than objective sleep tendency associated with scores on

Ambrogetti A.	Royal Newcastle Hospital, NSW, Australia. lolson@mail.newcastle.edu.au	Sleepiness Scale scores, multiple sleep latency tests and psychological symptoms.	Dec;7(4):248-53	the Epworth Sleepiness Scale (ESS). There were 225 subjects, of whom 40% had obstructive sleep apnoea (OSA), 16% had simple snoring, and 4.9% had snoring with sleep disruption (upper airway resistance syndrome); 9.3% had narcolepsy and 7.5% had hypersomnolence without REM sleep abnormalities; 12% had chronic fatigue syndrome; 7.5% had periodic limb movement disorder and 3% had diurnal rhythm disorders. ESS, the results of overnight polysomnography and multiple sleep latency test (MSLT) and SCL-90 as a measure of psychological symptoms were recorded. The ESS score and the mean sleep latency (MSL) were correlated (Spearman rho = -0.30, P < 0.0001). The MSL was correlated with total sleep time (TST) and with sleep efficiency but not with apnoea/hypopnoea index. There was no association between the MSL and any aspect of SCL-90 scores, except a borderline significant association with the somatisation subscale. The ESS was correlated with TST but not with sleep efficiency or apnoea/hypopnoea index. The ESS was correlated with all subscales of the SCL-90 except psychoticism. An ESS > or = 10 had poor sensitivity and specificity as a predictor of MSL < 10 min or MSL < 5 min. We conclude that the MSLT and the ESS are not interchangeable. The ESS was influenced by psychological factors by which the MSL was not affected. The ESS cannot be used to demonstrate or exclude sleepiness as it is measured by MSLT.
Ottenweller JE, Natelson BH, Gause WC, Carroll KK, Beldowicz D, Zhou XD, LaManca JJ.	Neurobehavioral Unit, VA Medical Center, East Orange, NJ 07018-1095, USA. jeo@nbunj.jvnc.net	Mouse running activity is lowered by Brucella abortus treatment: a potential model to study chronic fatigue.	Physiol Behav 1998 Mar;63(5):795-801	Chronic fatigue syndrome, which can occur after acute infection and last for years, is characterized by severe and persistent fatigue. Others have reported decreases in mouse running activity following infection and have suggested this may provide an animal model for studying chronic fatigue. Voluntary running is a highly motivated activity in mice, which will often run 5-7 mi/day in our laboratory. Following 2 weeks of acclimation to running wheels with food and water available ad lib, female BALB/c mice received 0.2-mL tail vein injections of killed Brucella abortus (BA) or saline vehicle. Subsequently the effects on voluntary running and grooming behavior were determined. Injection of BA caused an immediate large decrease in running and a lack of grooming. Vehicle injections produced no changes in behavior. After the first several days of reduced running behavior, levels of running and grooming slowly returned back to normal over the next 2-4 weeks, with substantial individual differences in the rate of recovery. The pattern of running during recovery was intriguing in that BA mice first ran at normal levels just after the lights went out, but they stopped after only 1-2 h. As recovery proceeded, they gradually increased the duration of the running bout during the night. Because this model uses voluntary exertion and the ability to run for longer periods of time characterizes recovery, the model may be a good one for studying the biologic underpinnings of chronic fatigue.
Panay N, Studd JW.	Academic Department of Obstetrics and Gynaecology, Chelsea and Westminster Hospital, London, UK.	The psychotherapeutic effects of estrogens.	Gynecol Endocrinol 1998 Oct;12(5):353-65	The effect of estrogens on the central nervous system, particularly mood and behavior, remains a controversial area which needs clarification, not just for understanding of depression in women but to ensure that such commonplace problems in women have efficient and appropriate therapy. There is now good evidence that estrogens are rapidly effective in the treatment of depression in many women but this information has not found its way through to those health care personnel, psychiatrists and psychologists who are principally involved in the treatment of depression. There is also strong evidence for the benefits of estrogens on cognitive functioning, not only in preventing the onset of dementia but also in improving the symptoms in the established condition. Recent work has also suggested a benefit for estrogens on mood in women diagnosed as suffering from chronic fatigue syndrome. This article reviews the effect of endogenous estrogen on the female central nervous system and the ever increasing evidence for the diverse psychotherapeutic effects of exogenous estrogens.
Patarca R, Mary Ann Fletcher		Interleukin-6 and Disease Two Case Reports that Point to the Usefulness of Measuring Cytokine Levels in Clinical Settings	Journal of Chronic Fatigue Syndrome 1998; 4(1): 53 - 69	Chronic fatigue syndrome has been associated with patterns of cytokine imbalances whose relevance to disease status remains to be documented. We present here two case reports that illustrate the relevance of measuring interleukin-6 levels in biological fluids in two clinical entities: hypothermia and Sjögren's syndrome. Further studies of this nature in extended patient populations will allow to discern the relevant contribution among the pleiotropy of roles of each particular cytokine in different clinical settings. It becomes apparent from the cases presented that the clinical manifestation of the imbalance in the expression of a particular cytokine is contingent upon the compartment where it occurs and upon levels of other cytokines. Similar studies will allow to define signature cytokine imbalances for each disease condition and may also shed light on thus far uncharacterized etiological agents.
Peterson PK, Pheley A, Schroepel J, Schenck C, Marshall P, Kind A,	Department of Medicine, Hennepin County Medical Center, Minneapolis, Minn	A preliminary placebo- controlled crossover trial of fludrocortisone for chronic	Arch Intern Med 1998 Apr 27;158(8):908-14Comment in: Arch Intern Med. 1998	OBJECTIVE: To provide a preliminary assessment of the efficacy and safety of fludrocortisone acetate treatment of chronic fatigue syndrome. DESIGN: A placebo-controlled, double-blind, random-allocation crossover trial of 6 weeks of fludrocortisone. SETTING: An outpatient clinical trials unit. PATIENTS:

Haugland JM, Lambrecht LJ, Swan S, Goldsmith S.	55415, USA. peter137@maroon.tc.umn.edu	fatigue syndrome.	Nov 9;158(20):2266-7	Twenty-five participants with chronic fatigue syndrome (mean age, 40 years; 19 [76%] women; mean duration of illness, 7.0 years) were recruited from a research and clinic registry. Five patients withdrew from the trial. INTERVENTIONS: All participants were scheduled to receive fludrocortisone acetate (0.1-0.2 mg) or a placebo for 6 weeks in each treatment. MAIN OUTCOME MEASURES: Self-administered questionnaires were completed at the beginning and end of each treatment arm that asked patients to rate the severity of their symptoms on a visual analogue scale. The Medical Outcomes Study 36-Item Short-Form Health Survey, a reaction time test, and a treadmill exercise test were used to assess functional status. Blood pressure, heart rate, and plasma norepinephrine levels were obtained at baseline. Blood pressure and heart rate were recorded at the end of the exercise test and monitored at all subsequent visits. RESULTS: At baseline, the study participants reported symptom severity greater than 5 for most symptoms, and all had evidence of marked functional impairments. No improvement was observed in the severity of any symptom or in any test of function for the 20 participants who completed both arms of the trial. Blood pressure and heart rate readings were unaffected by treatment, and plasma norepinephrine levels did not differ from those of a healthy control group. The incidence of adverse experiences was similar in the fludrocortisone and placebo arms of the trial. CONCLUSION: Low-dose fludrocortisone does not provide sufficient benefit to be evident in a preliminary blinded trial of unselected patients with chronic fatigue syndrome. Publication Types: Clinical Trial Randomized Controlled Trial
Pollet C, Natelson BH, Lange G, Tiersky L, DeLuca J, Policastro T, Desai P, Ottenweller JE, Korn L, Fiedler N, Kipen H.	Center for Environmental Hazards Research, VA Medical Center, East Orange, NJ 07018, USA.	Medical evaluation of Persian Gulf veterans with fatigue and/or chemical sensitivity.	J Med 1998;29(3-4):101-13	The purpose of this study was to determine if Gulf War veterans with complaints of severe fatigue and/or chemical sensitivity (n = 72) fulfill case definitions for chronic fatigue syndrome (CFS) and/or multiple chemical sensitivity (MCS) and to compare the characteristics of those veterans who received a diagnosis of CFS (n = 24) to a group of non-veterans diagnosed with CFS (n = 95). Thirty-three veterans received a diagnosis of CFS with 14 having MCS concurrently; an additional six had MCS but did not fulfill a case definition for CFS. The group of fatigued veterans receiving a diagnosis of CFS was comprised of significantly fewer women and fewer Caucasians than the civilian group, and significantly fewer veterans reported a sudden onset to their illness. Veterans with CFS had a milder form of the illness than their civilian counterparts based on medical examiner assessment of the severity of the symptoms, reported days of reduced activity, and ability to work. Since CFS in veterans seems less severe than that seen in civilians, the prognosis for recovery of veterans with this disorder may be better.
Poteliakhoff A		Fatigue Syndromes and the Aetiology of Autoimmune Disease	Journal of Chronic Fatigue Syndrome 1998; 4(4): 31 - 49	In the last decade or so, an impairment of Hypothalamic-Pituitary-Adrenal (HPA) axis activity has been observed in fatigue syndromes. Elevated levels of glucocorticoids help to prevent the immune system from over-reacting and generating a damaging autoimmune process. The corollary should be that reduced activity of the HPA axis and diminished levels of plasma cortisol could be associated with autoimmune (AI) disease. Experimental work in mice and rats supports this view. Furthermore, plasma levels of cortisol have been found to be low in the early stages of rheumatoid arthritis. There is some clinical evidence that connective tissue disorders (many of which are regarded as autoimmune diseases) occur approximately one year after the onset of prolonged or chronic fatigue, with the implication that fatigue is not merely a symptom of these disorders but precedes them. Many workers have found changes in the immune system of subjects suffering from CFS (mainly immune activation) which could be conducive to the development of AI disease. It has recently been found that there is, in the CFS, some deficiency of another adrenal steroid, namely that of dehydroepiandrosterone. This steroid exerts a regulatory activity on the immune system and a deficiency may well be an additional factor in the genesis of AI disease. If an association can be established between fatigue syndromes and autoimmune disease then these syndromes will need to be addressed in a more concerned manner and prophylactic measures undertaken to forestall AI disease.
Richardson J, Durval Campos Costa		Relationship Between SPECT Scans and Buspirone Tests in Patients with ME/CFS	Journal of Chronic Fatigue Syndrome 1998; 4(3): 23 - 38	The purpose of this exercise was to study the relationship between the detail shown on the SPECT brain scans with those seen in the buspirone tests. Thirty-nine patients are included in this study. These patients were selected from a large number who had been referred to Dr. Richardson from various parts of the country by their doctors because of a tentative diagnosis of ME/CFS. All the selected patients were confirmed by Dr. Richardson as suffering from ME/CFS taking into account the subjective scoring methods, clinical examination, virology and buspirone tests. This study is an attempt to link together the results of the previously described techniques to investigate possible areas of impaired cellular function in brain which may have purely neuronal effects or possibly neurohormonal effects. All patients within this study displayed hypoperfusion in some brain area as shown by their SPECT scans (see Appendix, Table

				1.1). Thirty-five (90%) showed hypoperfusion in the regions comprising: Twenty-four (62%) in the Brain Stem Twenty (51%) in the Caudate Nuclei Nine (23%) showed hypoperfusion in both Brain Stem and Caudate Nuclei regions Thirty (77%) cases demonstrated hypoperfusion in the regions comprising: Twenty-four (62%) in the Temporal Lobes Twelve (31%) in the Parietal Lobes Nine (23%) in the Frontal Lobes. The significance of these results is to confirm that there is actual evidence of neurological dysfunction which results in the continuing morbidity in these ME/CFS patients. The completion of this buspirone test and SPECT scan can be deemed to be basic complementary evidence for the positive diagnosis of ME/CFS.
Rowbottom D, David Keast, , Zhukov Pervan, Carmel Goodman, Chotoo Bhagat Byron Kakulas Alan Morton		The Role of Glutamine in the Aetiology of the Chronic Fatigue Syndrome A Prospective Study	Journal of Chronic Fatigue Syndrome 1998; 4(2): 3 - 22	Background: Recent studies have observed low plasma glutamine concentrations in chronic fatigue syndrome (CFS) subjects. Glutamine has been shown to be essential for immune function and a key substrate in brain neurochemistry. A dysfunctional immune response to infection and/or neurotransmitter dysfunction may be associated with CFS. Objective: To compare the glutamine status of CFS subjects to matched controls and to test the effect of L-glutamine supplementation on the symptoms associated with CFS. Design: A 26-week, randomised, double-blind, placebo-controlled trial. Patients: Sixteen subjects diagnosed with CFS and 16 age and sex-matched, healthy controls. Intervention: L-glutamine or placebo (2000 mg/day for 26 weeks). Measurements: Plasma and muscle glutamine concentrations, complete haematology counts, lymphocyte surface marker analysis, serum cortisol and testosterone concentrations, and self-reported symptomatic status. Results: Plasma and muscle glutamine concentrations were lower in CFS subjects than controls ($P < 0.001$ and $P = 0.027$, respectively). Significant increases in plasma ($P = 0.020$) and muscle ($P = 0.037$) glutamine concentration were observed following L-glutamine, but not placebo ($P > 0.05$), supplementation. However, improvements in symptomatic status were not observed in the L-glutamine group. Although six subjects showed clinical improvements during the trial, there was no change in their plasma or muscle glutamine concentrations. Conclusions: These data suggest that while low plasma glutamine concentrations may occur coincident with CFS, they may not be directly causative of fatigue or other symptoms.
Rowbottom D, David Keast, Zhukov Pervan, Alan Morton		The Physiological Response to Exercise in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998; 4(2): 33 - 49	Background: The chronic fatigue syndrome (CFS) is characterised by a limited exercise capacity. Studies have reported reduced muscle oxidative capacity in CFS, evidenced by abnormal acidosis during exercise and reduced aerobic capacity and exercise endurance. Objective: To compare physiological responses to walking exercise in CFS subjects, sedentary controls, and clinically improved CFS subjects. Design: Age and sex-matched pairs, with repeated measures. Subjects: Sixteen subjects diagnosed with CFS and 16 age and sex-matched sedentary controls. Measurements: Heart rate (HR), oxygen uptake (VO_2), ventilation (VE) and relative perceived exertion (RPE) responses to incremental walking exercise to volitional exhaustion. Results: CFS subjects reached significantly lower HRpeak ($P = 0.023$) and achieved nonsignificantly ($P > 0.05$) lower VO_{2peak} than control subjects. Despite no differences in submaximal exercise responses, CFS subjects reported higher RPE scores than controls ($P = 0.003$) at submaximal workloads. RPE scores correlated with symptomatic scores for emotionality ($r = 0.642$) and general fatigue ($r = 0.568$). Symptomatic recovery in six CFS subjects was associated with nonsignificant increases in HRpeak, VO_{2peak} and VEpeak, and nonsignificant decreases in RPE scores at submaximal workloads. Conclusions: These data suggested that the limited exercise capacity in CFS subjects may be explained by deconditioning due to the sedentary lifestyle necessitated by the condition, coupled with an increased perception of exertion, potentially linked to psychological symptoms associated with CFS.
Rowbottom DG, Keast D, Green S, Kakulas B, Morton AR.	Department of Human Movement, University of Western Australia, Nedlands, Australia.	The case history of an elite ultra-endurance cyclist who developed chronic fatigue syndrome.	Med Sci Sports Exerc 1998 Sep;30(9):1345-8	An elite ultra-endurance athlete, who had previously undergone physiological and performance testing, developed chronic fatigue syndrome (CFS). An incremental cycling exercise test conducted while he was suffering from CFS indicated decreases in maximum workload achieved (W_{max} ; -11.3%), the maximum oxygen uptake (VO_{2max} ; -12.5%), and the anaerobic threshold (AT; -14.3%) compared to pre-CFS data. A third test conducted after the athlete had shown indications of significant improvement in his clinical condition revealed further decreases in W_{max} (-7.9%), VO_{2max} (-10.2%) and AT (-8.3%). These data, along with submaximal exercise data and muscle biopsy electron microscopic analyses, suggest that the performance decrements were the result of detraining, rather than an impairment of aerobic metabolism due to CFS per se. These data may be indicative of central, possibly neurological, factors influencing fatigue perception in CFS sufferers.
Rowe PC, Calkins H.	Department of Pediatrics, Johns Hopkins University	Neurally mediated hypotension and chronic	Am J Med 1998 Sep 28;105(3A):15S-21S	A substantial body of clinical evidence now supports an association between various forms of hypotension and both idiopathic chronic fatigue and the chronic fatigue syndrome (CFS). Patients with CFS have a high

	School of Medicine, Baltimore, Maryland, USA.	fatigue syndrome.		prevalence of neurally mediated hypotension, and open treatment of this autonomic dysfunction has been associated with improvements in CFS symptoms. Randomized trials are now in progress to evaluate the efficacy of treatments directed at neurally mediated hypotension in those with CFS patients, and the results of these trials should help guide more basic inquiries into the mechanisms of orthostatic intolerance in affected individuals.
Russo J, Katon W, Clark M, Kith P, Sintay M, Buchwald D.	Department of Psychiatry & Behavioral Sciences, Harborview Medical Center, University of Washington, Seattle 98104, USA. jerusso@u.washington.edu	Longitudinal changes associated with improvement in chronic fatigue patients.	J Psychosom Res 1998 Jul;45(1 Spec No):67-76	Tertiary care patients with chronic fatigue were followed for 2.5 years to determine if changes in physical and psychological status were associated with improvements in chronic fatigue, physical functioning, and return to work. Results indicated that improvement in psychological symptoms, DSM-III-R disorders, physical examination signs, and changes in whether the patient continued to meet criteria for chronic fatigue syndrome (CFS) were associated with recovery from fatigue, improved functioning, and return to work. Patients who never met CFS criteria or only met criteria at the initial assessment, reported improved physical functioning. Patients whose psychiatric disorders and physical examination signs were still present at a mean follow-up time of 2.5 years were more likely to have persistent fatigue and work disability. Loss of physical examination signs was a significant independent predictor of improved functioning and return to work. These results suggest that psychiatric status, as well as physical status, are associated with recovery from chronic fatigue.
Saggini R, Pizzigallo E, Vecchiet J, Macellari V, Giacomozzi C.	Institute of Medical Pathophysiology, University G. D'Annunzio, Chieti, Italy.	Alteration of spatial-temporal parameters of gait in Chronic Fatigue Syndrome patients.	J Neurol Sci 1998 Jan 21;154(1):18-25	Chronic Fatigue Syndrome (CFS) has been widely studied and a lot of information is available in the literature regarding the immunological, virological, neuroendocrinal and psychiatric aspects of the disease, but its aetiology is still poorly understood. Great attention has also been paid to the alteration of the muscular function caused by CFS. The aim of the present work was to study CFS patients' gait in order to find out objective measures which can better characterize the pathology. Spatial and temporal parameters of gait were collected from a group of 12 CFS informed volunteers by using the typical instrumentation of movement analysis, and raw data were statistically elaborated. Comparisons with reference data from a population of healthy subjects revealed significant abnormalities in the symmetry indices of the bilateral parameters and in the linear relationships among parameters, and between these parameters and the physical characteristics of the patients. Interestingly, the abnormalities were present as from the beginning of the gait, which indicates that they are unlikely to be caused by the rapid increasing fatigue. This strengthens the hypothesis of a direct involvement of the central nervous system (CNS) in the onset of the disease.
Saltzstein BJ, Wyshak G, Hubbuch JT, Perry JC.	Harvard Medical School, Boston, MA, USA.	A naturalistic study of the chronic fatigue syndrome among women in primary care.	Gen Hosp Psychiatry 1998 Sep;20(5):307-16	Chronic fatigue syndrome (CFS), a controversial illness without clear etiology, causes profound debilitation in its sufferers. This study explored subjects' perceptions of the variables that mediated the course of their illness and identified coping strategies in 15 women with CFS referred from the practice of a primary care physician. Exploratory semistructured interviews were adapted from Kleinman's Illness Narratives. Four instruments were used: the Beck Depression Inventory, the Sickness Impact Profile, a modified Karnofsky scale, and the Defense Mechanism Rating Scale. Of the 15 women, 60% reported improvement and/or recovery at the time of the interview. Improvement was associated with social support and lower levels of depressive symptoms. Health status was influenced by how subjects perceived their illness, their future, and the doctor's prognosis; and by the physician's early diagnosis, validation of the CFS, and intensive medical follow-up. Obsessional and healthy neurotic defense levels predominated, which differs from historical comparison groups with dysthymia and panic disorder. Psychological adaptation to CFS is similar to adaptive coping in other chronic illnesses: subjective perceptions of health status can predict functional status. Physician validation is particularly important given the controversial status of CFS. Maintaining relationships with others--doctor, work, family, and group/spiritual activities reflected healthy coping strategies that promoted hope and attitudinal shifts. The finding of a mixture of neurotic and healthy defenses and a low proportion of defenses associated with personality disorders has not been previously reported in the CFS literature and warrants further investigation.
Schmalig KB, Daniel L. Hamilos Jeannie D. DiClementi, James F. Jones		Pain Perception in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(3): 13 - 22	Pain complaints (myalgia, arthralgia, headache, sore throat) are commonly associated with chronic fatigue syndrome (CFS), yet to date, these patients' responses to standardized measures of pain perception have not been investigated. Pain perception was measured by pressure dolorimeter and ice water cold pressor tests, and the McGill Pain Questionnaire among 15 female subjects with CFS, 11 subjects with Major Depression and 11 healthy controls. No differences were found between the groups for pain threshold or intolerance levels on the pressure dolorimeter and cold pressor tests. CFS and depressed subjects endorsed significantly

				more self-reported pain complaints than did control subjects. Although more pain complaints were predicted by greater somatization and lower health perceptions, pain threshold and intolerance were not associated with psychiatric symptoms or functional status. The study yielded some interesting preliminary observations related to variability in pain tolerance among CFS patients. These preliminary observations are discussed in terms of the need for future research and their potential implications for treatment and coping with the illness.
Scott LV, Burnett F, Medbak S, Dinan TG.	Department of Psychological Medicine, St Bartholomew's and the Royal London School of Medicine.	Naloxone-mediated activation of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome.	Psychol Med 1998 Mar;28(2):285-93	BACKGROUND: Opioidergic pathways have an inhibitory regulatory influence on the hypothalamic-pituitary-adrenal axis (HPA) in man. Previous studies have suggested impairment of pituitary-adrenal activation in chronic fatigue syndrome (CFS). We, therefore, decided to investigate the extent of opioid inhibition of HPA activity in CFS as a possible explanation for the reputed HPA hypofunctioning in patients with CFS. METHOD: Thirteen patients with CFS, diagnosed according to CDC criteria, were compared with thirteen healthy subjects. Adrenocorticotropin (ACTH) and cortisol (CORT) responses were measured following the administration of the opiate antagonist naloxone. RESULTS: Baseline ACTH and cortisol levels did not differ between the two groups. The release of ACTH (but not cortisol) was significantly blunted in the CFS subjects compared with controls. CONCLUSIONS: Naloxone mediated activation of the HPA is attenuated in CFS. Excessive opioid inhibition of the HPA is thus an unlikely explanation for the HPA dysregulation in this disorder.
Scott LV, Dinan TG.	Department of Psychological Medicine, St. Bartholomew's Hospital and the Royal London School of Medicine, West Smithfield, UK.	Urinary free cortisol excretion in chronic fatigue syndrome, major depression and in healthy volunteers.	J Affect Disord 1998 Jan;47(1-3):49-54	Urinary free cortisol excretion (UFC) was compared in 21 patients with chronic fatigue syndrome (CFS), in 10 melancholic depressives and in 15 healthy controls. Patients with depression had UFC values which were significantly higher than healthy comparison subjects, whereas UFC excretion of CFS patients was significantly lower than the comparison group. These findings are in keeping with currently held hypotheses of hyperactivity and hypoactivity of the hypothalamic-pituitary-adrenal (HPA) axis in depression and chronic fatigue syndrome respectively. Five of the 21 CFS patients had a co-morbid depressive illness. This sub-group retained the profile of UFC excretion of those with CFS alone, suggesting a different pathophysiological basis for depressive symptoms in CFS.
Scott LV, Medbak S, Dinan TG.	Department of Psychological Medicine, St Bartholomew's and the Royal London School of Medicine, West Smithfield, UK.	Blunted adrenocorticotropin and cortisol responses to corticotropin-releasing hormone stimulation in chronic fatigue syndrome.	Acta Psychiatr Scand 1998 Jun;97(6):450-7	Hypofunctioning of the pituitary-adrenal axis has been suggested as the pathophysiological basis for chronic fatigue syndrome (CFS). Blunted adrenocorticotropin (ACTH) responses but normal cortisol responses to exogenous corticotropin-releasing hormone (CRH), the main regulator of this axis, have been previously demonstrated in CFS patients, some of whom had a comorbid psychiatric disorder. We wished to re-examine CRH activation of this axis in CFS patients free from concurrent psychiatric illness. A sample of 14 patients with CDC-diagnosed CFS were compared with 14 healthy volunteers. ACTH and cortisol responses were measured following the administration of 100 microg ovine CRH. Basal ACTH and cortisol values did not differ between the two groups. The release of ACTH was significantly attenuated in the CFS group ($P < 0.005$), as was the release of cortisol ($P < 0.05$). The blunted response of ACTH to exogenous CRH stimulation may be due to an abnormality in CRH levels with a resultant alteration in pituitary CRH receptor sensitivity, or it may reflect a dysregulation of vasopressin or other factors involved in HPA regulation. A diminished output of neurotrophic ACTH, causing a reduced adrenocortical secretory reserve, inadequately compensated for by adrenoceptor upregulation, may explain the reduced cortisol production demonstrated in this study.
Scott LV, Medbak S, Dinan TG.	Department of Psychiatry, Trinity College Medical School, Dublin, Eire.	The low dose ACTH test in chronic fatigue syndrome and in health.	525: Clin Endocrinol (Oxf) 1998 Jun;48(6):733-7 Comment in: Clin Endocrinol (Oxf). 2000 Jun;52(6):797-9	OBJECTIVE: A number of dynamic tests of the hypothalamic-pituitary-adrenal axis provide evidence for a mild central adrenal insufficiency in chronic fatigue syndrome (CFS). The 1 microgram adrenocorticotropin (ACTH) test has been proposed to be more sensitive than the standard 250 micrograms ACTH test in the detection of subtle pituitary-adrenal hypofunctioning. We aimed to establish whether the 1 microgram ACTH test would support such a dysregulation in CFS, and also, given the relative novelty of this test in clinical practice and the uncertainty with regard to appropriate cut-off values for normality, to compare our healthy volunteer data with those of previous studies. PATIENTS AND DESIGN: Twenty subjects with CFS, diagnosed according to Centres for Disease Control and Prevention criteria, were compared with 20 healthy volunteer subjects. All participants underwent a 1 microgram ACTH test beginning at 1400 h. Plasma samples for cortisol estimation were drawn at 0, and min. RESULTS: Baseline cortisol values did not differ between CFS patients and healthy subjects. The delta cortisol (maximum increment from baseline) value was significantly lower in the CFS than the volunteer group ($P < 0.05$). Comparison of the min cortisol values revealed no significant differences. Using an incremental cortisol of > 250 nmol/l as an

				arbitrary cutoff point, two (10%) of the healthy subjects and nine (45%) of the CFS subjects failed the test on this basis ($\chi^2 = 4.3$, $df = 38$, $P < 0.05$). CONCLUSIONS: This study provides further evidence for a subtle pituitary-adrenal insufficiency in subjects with chronic fatigue syndrome compared to healthy volunteers. Disparities between our healthy volunteer data and those of other groups using the 1 microgram ACTH test suggest that the test may not be as reliable as previously indicated.
See DM, Cimoch P, Chou S, Chang J, Tilles J.	University of California, Irvine, Department of Medicine, Orange 92668, USA.	The in vitro immunomodulatory effects of glyconutrients on peripheral blood mononuclear cells of patients with chronic fatigue syndrome.	Integr Physiol Behav Sci 1998 Jul-Sep;33(3):280-7	In humans, eight monosaccharides are required for the synthesis of glycoproteins. Dietary supplements that supply these crucial sugars are known as glyconutrients. A glyconutrient compound was added to Peripheral Blood Mononuclear Cells (PBMC) isolated from normal controls and patients with the Chronic Fatigue Syndrome (CFS), a disease associated with immune dysregulation. The in vitro immunomodulatory effects were investigated. Cell surface expression of the glycoproteins CD5, CD8, and CD11a were significantly lower in patients with CFS compared to normal controls. Addition of glyconutrient homogenate to PBMC from patients with CFS stimulated with phytohemagglutinin significantly increased the expression of each glycoprotein. Furthermore, natural killer (NK) cell function was reduced in CFS patients. The glyconutrient preparation significantly enhanced NK cell activity versus human herpes virus 6 (HHV-6)-infected H9 cells in an 8 h ^{51}Cr release assay compared to placebo for PBMC from patients with CFS ($p < .01$). Finally, apoptosis was significantly higher in patients with CFS. The percentage of apoptotic cells was significantly decreased in PBMC from patients with CFS that had been incubated for 48 h with glyconutrients. Thus, glyconutrients improved abnormal immune parameters in vitro in patients with CFS.
Seelig M		Review and Hypothesis Might Patients with the Chronic Fatigue Syndrome Have Latent Tetany of Magnesium Deficiency	Journal of Chronic Fatigue Syndrome 1998; 4(2): 77 - 108	The latent tetany syndrome (LTS) parallels CFS in its neuromuscular and psychiatric manifestations, as well as in inner ear disturbances: vestibular in CFS and FM, as well as in LTS, and increased vulnerability to noise-induced deafness in LTS. Microvascular damage to the cochlea is seen in Mg deficiency, noise-induced deafness, and might be a factor in migraine and other severe headaches in both LTS and in CFS and FM. Abnormal sleep patterns occur in both LTS and CFS; impaired cognition more in CFS than in LTS. However, some brain and neurotransmitter dysfunctions seen with Mg deficiency might be contributory to cognitive disorders of CFS. Mg loss caused by enhanced catecholamine release produced by stress may well be contributory to stress-induced acute episodes of CFS. Malfunctions of the cellular and humoral immunological systems are caused by experimental Mg deficiency. Whether allergies in CFS patients and abnormal response to antigenic challenge are results of low Mg remains to be proven. Mitral valve prolapse is seen in many LTS and CFS patients; whether a putative Mg deficiency predisposes to this abnormality is not known. Clinical improvement with Mg treatment has been proven in LTS, and seemed helpful in the rare cases of CFS and FM in whom it has been tried. The Mg status should be determined in patient with CFS and FM, but methodology is a handicap. Serum Mg is an inaccurate index. Three methods show promise. Percentage retention of a Mg load is accurate but requires patient's cooperation. Free ionic Mg measurement requires ion-selective electrodes. Blood cell Mg is reliable in a little more than half the patients; sublingual cell Mg seems more accurate. More intensive, and controlled studies of the Mg status of CFS and FM patients, and of their response to Mg therapy is desirable.
Servatius RJ, Tapp WN, Bergen MT, Pollet CA, Drastal SD, Tiersky LA, Desai P, Natelson BH.	New Jersey Medical School, Department of Neuroscience, East Orange 07019, USA.	Impaired associative learning in chronic fatigue syndrome.	Neuroreport 1998 Apr 20;9(6):1153-7	Patients with chronic fatigue syndrome (CFS) report cognitive difficulties (impaired attention, memory and reasoning). Neuropsychological tests have failed to consistently find cognitive impairments to the degree reported by CFS patients. We tested patients with CFS and sedentary controls in protocols designed to measure sensory reactivity and acquisition of the classically conditioned eyeblink response. Patients with CFS exhibited normal sensitivity and responsiveness to acoustic stimuli. However, CFS patients displayed impaired acquisition of the eyeblink response using a delayed-type conditioning paradigm. Sensitivity and responsiveness to the airpuff stimulus were normal. In the absence of sensory/motor abnormalities, impaired acquisition of the classically conditioned eyeblink response indicates an associative deficit. These data suggest organic brain dysfunction within a defined neural substrate in CFS patients.
Sharpe M.		Doctors' diagnoses and patients' perceptions. Lessons from chronic fatigue syndrome.	Gen Hosp Psychiatry 1998 Nov;20(6):335-8	
Sharpe M.		Cognitive behavior therapy for chronic fatigue syndrome.	Am J Psychiatry 1998 Oct;155(10):1461-2 Comment on: Am J	

			Psychiatry. 1997 Mar;154(3):408-14	
Sharpe M.	University of Edinburgh Department of Psychiatry, Royal Edinburgh Hospital, United Kingdom.	Cognitive behavior therapy for chronic fatigue syndrome: efficacy and implications.	Am J Med 1998 Sep 28;105(3A):104S-109S	Cognitive behavior therapy (CBT) is a form of non-pharmacologic treatment. It is based on a model of chronic fatigue syndrome (CFS) that hypothesizes that certain cognitions and behavior may perpetuate symptoms and disability—that is, act as obstacles to recovery. Treatment emphasizes self-help and aims to help the patient to recover by changing these unhelpful cognitions and behavior. There is now good evidence from 2 independent randomized clinical trials to support the efficacy of CBT in patients with CFS. The treatment effect is substantial, although few patients are cured. The urgent clinical need is to make this form of treatment available to patients with CFS. One approach is to incorporate the principles of CBT into routine clinical practice. The preliminary evaluation of these simpler forms of CBT are promising, although the results of controlled trials are awaited. At present, intensive individual CBT administered by a skilled therapist remains the treatment of choice for patients with CFS.
Sibbald B.		Chronic fatigue syndrome comes out of the closet.	CMAJ 1998 Sep 8;159(5):537-41 Comment in: CMAJ. 1999 Mar 9;160(5):636, 638 CMAJ. 1999 Mar 9;160(5):638	An Alberta court ruling and new guidelines for physicians issued by the Quebec medical college are giving chronic fatigue syndrome a legitimacy it never before enjoyed. What will this mean for physicians?
Sisto SA, Tapp WN, LaManca JJ, Ling W, Korn LR, Nelson AJ, Natelson BH.	NJCFS Center, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, USA. sueann@nbunj.jvnc.net	Physical activity before and after exercise in women with chronic fatigue syndrome.	QJM 1998 Jul;91(7):465-73	We measured physical activity after strenuous exercise in 20 women with chronic fatigue syndrome (CFS), compared to 20 sedentary healthy volunteers who exercised no more than once per week. Activity was measured for 2 weeks using a portable waist-worn vertical accelerometer. After the first week of activity monitoring, all participants returned for a maximal treadmill test, followed by continued activity monitoring for the second week. Five activity measures were derived from the data: (i) average activity; (ii) total activity; (iii) duration of waking day; (iv) duration; and (v) number of daily rests. A repeated measures ANCOVA was used to determine post-treadmill group differences accounting for pre-treadmill differences. There was a significant reduction in overall average activity after the treadmill test, with the greatest decrease on days 12 through 14. This reduction was accompanied by a significant increase in the duration of the waking day and number of daily rests. Thus, marked exertion does produce changes in activity, but later than self-report would suggest, and are apparently not so severe that CFS patients cannot compensate.
Smit AA, Bolweg NM, Lenders JW, Wieling W.	Academisch Medisch Centrum, afd. Interne Genceskunde, Amsterdam.	[No strong evidence of disturbed regulation of blood pressure in chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneesk 1998 Mar 21;142(12):625-8	Recent medical publications postulate a connection between the Chronic Fatigue Syndrome (CFS) and disturbed regulation of the circulation, manifesting itself during orthostatic stress testing. Four studies were published on the circulatory response on prolonged head up tilt testing. Numerous CFS patients displayed postural tachycardia or syncope during the test. However, many CFS patients examined had had orthostatic symptoms prior to the examination. It is not certain that cardiovascular dysregulation is present in CFS patients without orthostatic symptoms. It is also not clear whether such a dysregulation would be the effect of physical inactivity or a manifestation of a subtle form of autonomic neuropathy.
Speight AN.		Increased illness experience preceding chronic fatigue syndrome.	J R Coll Physicians Lond 1998 May- Jun;32(3):274 Comment in: J R Coll Physicians Lond. 1998 Jul-Aug;32(4):389 and 1998 Jan-Feb;32(1):44-8	
Steele L, Dobbins JG, Fukuda K, Reyes M, Randall B, Koppelman M, Reeves WC.	Viral Exanthems and Herpesvirus Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, US Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.	The epidemiology of chronic fatigue in San Francisco.	Am J Med 1998 Sep 28;105(3A):83S-90S	Despite considerable research on chronic fatigue syndrome (CFS) and conditions associated with unexplained chronic fatigue (CF), little is known about their prevalence and demographic distribution in the population. The present study describes the epidemiology and characteristics of self-reported CF and related conditions in a diverse urban community. The study used a cross-sectional telephone screening survey of households in San Francisco, followed by interviews with fatigued and nonfatigued residents. Respondents who appeared to meet case definition criteria for CFS, based on self-reported fatigue characteristics, symptoms, and medical history, were classified as CFS-like cases. Subjects who reported idiopathic chronic fatigue (ICF) that did not meet CFS criteria were classified as ICF-like cases. Screening interviews were completed for 8,004 households, providing fatigue and demographic information for 16,970 residents. Unexplained CF was extremely rare among household residents <18 years of age, but was reported by 2% of adult respondents. A total of 33 adults (0.2% of the study population) were classified as

				CFS-like cases and 259 (1.8%) as ICF-like cases. Neither condition clustered within households. CFS- and ICF-like illnesses were most prevalent among women and persons with annual household incomes below \$40,000, and least prevalent among Asians. The prevalence of CFS-like illness was elevated among African Americans, Native Americans, and persons engaged in clerical occupations. Although CFS-like cases were more severely ill than those with ICF-like illness, a similar symptom pattern was observed in both groups. In conclusion, conditions associated with unexplained CF occur in all sociodemographic groups but appear to be most prevalent among women, persons with lower income, and some racial minorities.
Stewart J, Weldon A, Arlievsky N, Li K, Munoz J.	Department of Pediatrics, New York Medical College, Valhalla 10595, USA. stewart@nymc.edu	Neurally mediated hypotension and autonomic dysfunction measured by heart rate variability during head-up tilt testing in children with chronic fatigue syndrome.	Clin Auton Res 1998 Aug;8(4):221-30	Recent investigations suggest a role for neurally mediated hypotension (NMH) in the symptomatology of chronic fatigue syndrome (CFS) in adults. Our previous observations in children with NMH and syncope (S) unrelated to CFS indicate that the modulation of sympathetic and parasympathetic tone measured by indices of heart rate variability (HRV) is abnormal in children who faint during head-up tilt (HUT). In order to determine the effects of autonomic tone on HUT in children with CFS we performed measurements of HRV during HUT in 16 patients aged 11-19 with CFS. Data were compared to 26 patients evaluated for syncope and with 13 normal control subjects. After 30 minutes supine, patients were tilted to 80 degrees for 40 minutes or until syncope occurred. Time domain indices included RR interval, SDNN, RMSSD, and pNN50. An autoregressive model was used to calculate power spectra. LFP (.04-.15 Hz), HFP (.15-.40Hz), and TP (.01-.40Hz). Data were obtained supine (baseline) and after HUT. Thirteen CFS patients fainted (CFS, 5/13 pure vasodepressor syncope) and three patients did not (CFS-). Sixteen syncope patients fainted (S, all mixed vasodepressor-cardioinhibitory) and 10 did not (S-). Four control patients fainted (Control, all mixed vasodepressor-cardioinhibitory) and nine did not (Control-). Baseline indices of HRV were not different between Control and S, and between Control- and S-, but were depressed in S compared to S-. HRV indices were strikingly decreased in CFS patients compared to all other groups. With tilt, SDNN, RMSSD, and pNN50 and spectral indices decreased in all groups, remaining much depressed in CFS compared to S or control subjects. With HUT, sympathovagal indices (LFP/HFP, nLFP, and nHFP) were relatively unchanged in CFS, which contrasts with the increase in nLFP with HUT in all other groups. With syncope RMSSD, SDNN, LFP, TP, and HFP increased in S (and Control), suggesting enhanced vagal heart rate regulation. These increases were not observed in CFS patients. CFS is associated with NMH during HUT in children. All indices of HRV are markedly depressed in CFS patients, even when compared with already low HRV in S or Control patients. Sympathovagal balance does not shift toward enhanced sympathetic modulation of heart rate with HUT and there is blunting in the overall HRV response with syncope during HUT. Taken together these data may indicate autonomic impairment in patients with CFS.
Stores G, Fry A, Crawford C.	University Section, Park Hospital for Children, Oxford, UK.	Sleep abnormalities demonstrated by home polysomnography in teenagers with chronic fatigue syndrome.	J Psychosom Res 1998 Jul;45(1 Spec No):85-91	To provide objective information about sleep physiology in young people with chronic fatigue syndrome (CFS), home polysomnography (PSG) was performed on 18 teenagers, aged 11-17 years, in whom CFS had been diagnosed according to internationally accepted criteria. The results were compared with those for healthy controls matched individually for gender and age. Compared with controls, CFS subjects showed significantly higher levels of sleep disruption by both brief and longer awakenings. Disruption of sleep in this way could at least contribute to the daytime symptoms of young people with CFS. The underlying cause of the disruption needs to be considered in each individual case. Further research is required to clarify the relative contribution of this neurobiological aspect of CFS in young people.
Streeten DH, Anderson GH Jr.	Department of Medicine, SUNY Health Science Center, Syracuse, NY 13210, USA.	The role of delayed orthostatic hypotension in the pathogenesis of chronic fatigue.	Clin Auton Res 1998 Apr;8(2):119-24	Past studies have shown that severe fatigue was the presenting symptom in six of seven patients with delayed orthostatic hypotension and that tilt table-induced hypotension was found in 22 of 23 patients with the chronic fatigue syndrome. We have determined the prevalence of fatigue, volunteered in response to a nonspecific pre-examination questionnaire used in 431 patients, each subsequently diagnosed as having one of eight neurological or endocrine disorders. The results show that fatigue is a very common symptom in patients with delayed orthostatic hypotension (n = 21), as well as both primary (n = 30) and secondary (n = 106) hypocortisolism: 70-83% in all groups. In contrast, fatigue was an uncommon complaint in patients with multiple system atrophy (MSA) (n = 30), pituitary disorders without hypocortisolism (n = 106) or idiopathic hirsutism (n = 96): 7-33% in all groups, and was intermediate in prevalence in patients with acute hyperadrenergic orthostatic hypotension (n = 32): 41%. It is concluded that fatigue commonly results from delayed orthostatic hypotension and all forms of hypocortisolism but is less common in patients with acute orthostatic hypotension, both idiopathic and due to MSA, which more commonly present with lightheadedness or syncope.

Streeten DH, David S. Bell		Original Research Circulating Blood Volume in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998; 4(1): 3 - 11	Chronic fatigue syndrome (CFS) is an illness associated with severe activity limitation and a characteristic pattern of symptoms despite a relatively normal physical examination and routine laboratory evaluation. The recent description of delayed orthostatic hypotension in patients with CFS, and previous findings of reduced red blood cell (RBC) mass in other patients with orthostatic hypotension not known to have CFS, led us to measure RBC mass and plasma volume in 19 individuals (15 female, four male) with well characterized, severe CFS. RBC mass was found to be significantly reduced ($p < 0.001$) below the published normal range in the 16 women, being subnormal in 15 (93.8%) of them as well as in two of the four men. Plasma volume was subnormal in 10 (52.6%) patients and total blood volume was below normal in 12 (63.2%). The high prevalence and frequent severity of the low RBC mass suggest that this abnormality might contribute to the symptoms of CFS by reducing the oxygen-carrying power of the blood reaching the brain in many of these patients.
Strickland P, Morriss R, Wearden A, Deakin B.	University of Manchester and (Guild NHS Trust), Department of Community Psychiatry, Royal Preston Hospital, Fulwood, UK.	A comparison of salivary cortisol in chronic fatigue syndrome, community depression and healthy controls.	J Affect Disord 1998 Jan;47(1-3):191-4	BACKGROUND: Previous studies reporting cortisol hyposecretion in chronic fatigue syndrome may have been confounded by venepuncture, fasting and hospitalisation. METHODS: Morning and evening salivary cortisol were obtained on consecutive days in the first 3 days of the menstrual cycle and compared in three samples of women taking no medication and matched for age: 14 patients with chronic fatigue syndrome, 26 community cases of ICD-10 current depressive episodes and 131 healthy community controls. RESULTS: The mean evening cortisol was significantly lower in the chronic fatigue syndrome patients compared to controls with depression ($P = 0.02$) and healthy controls ($P = 0.005$). Chronic fatigue syndrome patients without psychiatric disorder had significantly lower morning salivary cortisols compared to controls ($P = 0.009$). CONCLUSION: Chronic fatigue syndrome patients display cortisol hyposecretion in saliva as well as plasma compared to patients with depression and healthy controls. LIMITATIONS: Small samples of female patients with cortisol estimated at only two time points in the day. Cortisol secretion may be secondary to other neurotransmitter abnormalities or other physiological or lifestyle factors in chronic fatigue syndrome patients. CLINICAL RELEVANCE: Chronic fatigue syndrome is biochemically distinct from community depression.
Swanink CM, Stolk-Engelaar VM, van der Meer JW, Vercoulen JH, Bleijenberg G, Fennis JF, Galama JM, Hoogkamp-Korstanje JA.	Department of Medical Microbiology, University Hospital Nijmegen, The Netherlands.	Yersinia enterocolitica and the chronic fatigue syndrome.	J Infect 1998 May;36(3):269-72	OBJECTIVES: To investigate the potential role of Yersinia enterocolitica in patients with chronic fatigue syndrome (CFS). METHODS: An immunoblot technique was used to detect antibodies to various Yersinia outer membrane proteins (YOPs) in serum samples from 88 patients with CFS and 77 healthy neighbourhood controls, matched for gender and age. RESULTS: The prevalence of IgG and IgA antibodies to various Yersinia outer membrane proteins (YOPs) did not differ between patients with CFS and healthy controls. Twenty-four patients (27%) and nineteen controls (25%) had IgG antibodies to one or more YOPs. Four patients and two controls had both serum IgG and IgA antibodies to at least two different YOPs, compatible with a recent or persistent infection. Although all patients with positive IgG and IgA reactions to two or more YOPs had symptoms that could point to persistent Yersinia infection, these symptoms were also found frequently in patients without antibodies to YOPs. CONCLUSIONS: We conclude that Y. enterocolitica is unlikely to play a major role in the aetiology of CFS.
Terman M, Levine SM, Terman JS, Doherty S.	Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York State Psychiatric Institute, New York 10032, USA.	Chronic fatigue syndrome and seasonal affective disorder: comorbidity, diagnostic overlap, and implications for treatment.	Am J Med 1998 Sep 28;105(3A):115S-124S	This study aimed to determine symptom patterns in patients with chronic fatigue syndrome (CFS), in summer and winter. Comparison data for patients with seasonal affective disorder (SAD) were used to evaluate seasonal variation in mood and behavior, atypical neurovegetative symptoms characteristic of SAD, and somatic symptoms characteristic of CFS. Rating scale questionnaires were mailed to patients previously diagnosed with CFS. Instruments included the Personal Inventory for Depression and SAD (PIDS) and the Systematic Assessment for Treatment Emergent Effects (SAFTEE), which catalogs the current severity of a wide range of somatic, behavioral, and affective symptoms. Data sets from 110 CFS patients matched across seasons were entered into the analysis. Symptoms that conform with the Centers for Disease Control and Prevention (CDC) case definition of CFS were rated as moderate to very severe during the winter months by varying proportions of patients (from 43% for lymph node pain or enlargement, to 79% for muscle, joint, or bone pain). Fatigue was reported by 92%. Prominent affective symptoms included irritability (55%), depressed mood (52%), and anxiety (51%). Retrospective monthly ratings of mood, social activity, energy, sleep duration, amount eaten, and weight change showed a coherent pattern of winter worsening. Of patients with consistent summer and winter ratings ($n = 73$), 37% showed high global seasonality scores ($GSS > \text{or} = 10$). About half this group reported symptoms indicative of major depressive disorder, which was strongly associated with high seasonality. Hierarchical cluster

				analysis of wintertime symptoms revealed 2 distinct clinical profiles among CFS patients: (a) those with high seasonality, for whom depressed mood clustered with atypical neurovegetative symptoms of hypersomnia and hyperphagia, as is seen in SAD; and (b) those with low seasonality, who showed a primary clustering of classic CFS symptoms (fatigue, aches, cognitive disturbance), with depressed mood most closely associated with irritability, insomnia, and anxiety. It appears that a subgroup of patients with CFS shows seasonal variation in symptoms resembling those of SAD, with winter exacerbation. Light therapy may provide patients with CFS an effective treatment alternative or adjunct to antidepressant drugs.
Thompson D, Hylan TR, McMullen W, Romeis ME, Buesching D, Oster G.	Policy Analysis, Inc., Indianapolis, USA. dthompson@pai2.com	Predictors of a medical-offset effect among patients receiving antidepressant therapy.	Am J Psychiatry 1998 Jun;155(6):824-7	OBJECTIVE: Characteristics of patients receiving antidepressant therapy were examined to identify factors that may be associated with a medical-offset effect. METHOD: In a retrospective study, the authors analyzed claims data from a large health insurer in New England. The study subjects included 1,661 persons initiating treatment for depression with selective serotonin reuptake inhibitors or tricyclic antidepressants between July 1991 and June 1993. RESULTS: Patients with anxiety disorders, coronary heart disease, cancer, and chronic fatigue syndrome and those remaining on their initial regimens of antidepressant therapy for at least 6 months were more likely to experience significant reductions in the costs of medical care services. The number of visits to mental health providers had no effect on the costs of medical services. CONCLUSIONS: Specific comorbid conditions and sustained use of antidepressant drugs may be associated with a medical-offset effect for patients receiving treatment for depression.
Timothy K. Roberts , Neil R. McGregor, R. Hugh Dunstan, Mark Donohoe, Raymond N. Murdoch , D. Hope , DipEd, S. Zhang BMed, Henry L. Butt , Jennifer A. Watkins , Warren G. Taylor		Immunological and Haematological Parameters in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(4): 51 - 65	Red and white blood cell parameter profiles and pokeweed mitogen responses were investigated in 57 CDC-defined CFS patients and 34 age- and sex-matched controls. CFS patients had significantly different red and white blood cell profiles compared with controls. Red cell distribution width (RDW) was the primary regression factor differentiating the groups. RDW was positively associated with mean platelet volume (MPV) in control subjects, but negatively correlated with MPV in CFS patients, indicating a reversal of the functional relationship between these parameters in CFS patients. Hematological parameters, and not the immunological parameters studied, were more important in differentiating CFS patients from healthy control subjects. Female CFS patients had significant increases in RDW and mean platelet volume, and decreases in the numbers of T-helper cells, T-cells and lymphocytes compared with control females. These alterations were not observed in corresponding male comparisons. There were no differences in the pokeweed mitogen (PWM) response between the CFS and control groups. However, in control subjects, a significant association was observed between pokeweed mitogen responses and Rh(D) antigen status, whereas no similar association was measured in CFS patients. Rh(D)-negative control subjects had a significantly increased mitogen response compared with Rh(D)-positive subjects, whereas in CFS patients, no difference was found. It was concluded that future blood parameter and lymphocyte mitogen response studies in CFS patients should be controlled for sex and Rh status, respectively.
Tirelli U, Chierichetti F, Tavio M, Simonelli C, Bianchin G, Zanco P, Ferlin G.	Division of Medical Oncology and Acquired Immunodeficiency Syndrome, Centro di Riferimento Oncologico, Aviano, Italy.	Brain positron emission tomography (PET) in chronic fatigue syndrome: preliminary data.	Am J Med 1998 Sep 28;105(3A):54S-58S	Chronic fatigue syndrome (CFS) has been widely studied by neuroimaging techniques in recent years with conflicting results. In particular, using single-photon emission computed tomography (SPECT) and perfusion tracers, hypoperfusion has been found in several brain regions, although the findings vary across research centers. The objective of this study was to investigate brain metabolism of patients affected by CFS, using [18F]fluorine-deoxyglucose (18FDG) positron emission tomography (PET). We performed 18FDG PET in 18 patients who fulfilled the criteria of the working case definition of CFS. Twelve of the 18 patients were females; the mean age was 34.15 years (range, 15-68) and the median time from CFS diagnosis was 16 months (range, 9-138). Psychiatric diseases and anxiety/neurosis were excluded in all CFS patients. CFS patients were compared with a group of 6 patients affected by depression (according to DSM IV-R) and 6 age-matched healthy controls. The CFS patients were not taking any medication at the time of PET, and depressed patients were drug-free for at least 1 week before the PET examination. The PET images examined 22 cortical and subcortical areas. CFS patients showed a significant hypometabolism in right mediofrontal cortex (P = 0.010) and brainstem (P = 0.013) in comparison with the healthy controls. Moreover, comparing patients affected by CFS and depression, the latter group showed a significant and severe hypometabolism of the medial and upper frontal regions bilaterally (P = 0.037-0.001), whereas the metabolism of brain stem was normal. Brain 18FDG PET showed specific metabolism abnormalities in patients with CFS in comparison with both healthy controls and depressed patients. The most relevant result of our study is the brain stem hypometabolism which, as reported in a perfusion SPECT study, seems to be a marker for the in vivo diagnosis of CFS.

Treib J, Fernandez A, Haass A, Grauer MT, Holzer G, Woessner R.	Department of Neurology, University of the Saarland, Homburg, Germany.	Clinical and serologic follow-up in patients with neuroborreliosis.	Neurology 1998 Nov;51(5):1489-91 Comment in: Neurology. 1999 Sep 11;53(4):895-6	The authors performed a clinical and serologic follow-up study after 4.2 1.2 years in 44 patients with clinical signs of neuroborreliosis and specific intrathecal antibody production. All patients had been treated with ceftriaxone 2 g/day for 10 days. Although neurologic deficits decreased significantly, more than half the patients had unspecific complaints resembling a chronic fatigue syndrome and showed persisting positive immunoglobulin M serum titers for Borrelia in the Western blot analysis.
Tuck I, Human N.	Department of Nursing Systems, Community and Psychiatric Mental Health Nursing, School of Nursing, Virginia Commonwealth University, Richmond 23298-0567, USA.	The experience of living with chronic fatigue syndrome.	J Psychosoc Nurs Ment Health Serv 1998 Feb;36(2):15-9	1. Chronic fatigue syndrome (CFS) is a condition that affects the total person, body, mind, and spirit. 2. CFS sufferers describe the experience as being in the illness, remembering life before the illness, and living with the symptoms. 3. Empathy and compassion are essential components of providing nursing care for clients with CFS.
van de Luit L, van der Meulen J, Cleophas TJ, Zwinderman AH.	Department of Medicine, Merwede Hospital Dordrecht, The Netherlands.	Amplified amplitudes of circadian rhythms and nighttime hypotension in patients with chronic fatigue syndrome: improvement by inopamil but not by melatonin.	Angiology 1998 Nov;49(11):903-8	Fatigue is an important symptom of a disturbed circadian rhythm. To date, no studies of circadian rhythms in patients with chronic fatigue syndrome (CFS) have been published. The objectives of the study were to study rhythms of heart rate and systolic and diastolic blood pressure in patients with chronic fatigue syndrome compared with age-matched normotensive controls and to study the effects of melatonin and inopamil on such rhythms. Ambulatory blood pressure (ABP) measurements (Space Lab, Inc, validated) of 18 patients with CFS were made according to the 1987 U.S. Center for Disease Control Criteria, and measurements of 12 age-matched normotensive controls were used in a cosinor analysis of the two groups. The effects of melatonin and inopamil on ABP were studied subsequently in four patients in an 8-week open-label evaluation. One patient was hypertensive (diastolic blood pressure > 90 mm Hg at least once every 4 hours), and was, therefore, excluded. The data of the remaining 17 patients (15 women, 2 men) revealed a significant 12-hour rhythm in heart rate and 24-hour rhythm in systolic and diastolic blood pressure with 95% confidence intervals not significantly different from sinusoidal patterns. Although these rhythms were synchronous with the control group rhythms, their amplitudes were not and showed, respectively, 2.8, 2.8, and 9.0 times the size of the control group rhythms ($p < 0.001$, $p < 0.001$, and $p < 0.0001$, respectively). Systolic blood pressures in the patients with CFS were consistently below 100 mm Hg during the nighttime. In a subsequent pilot study of four patients from the study population treated with melatonin 4 mg daily and inopamil 200 mg daily for 4 weeks, inopamil reduced nighttime hypotension ($p < 0.05$), whereas melatonin increased nighttime hypotension ($p < 0.02$). Patients with CFS have increased amplitudes of circadian rhythms and systolic blood pressures consistently below 100 mm Hg during the nighttime. Positive inotropic compounds may be beneficial in such patients, but melatonin may not be.
Vercoulen JH, Bazelmans E, Swanink CM, Galama JM, Fennis JF, van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Hospital Nijmegen, The Netherlands. j.vercoulen@cksmpps.kun.nl	Evaluating neuropsychological impairment in chronic fatigue syndrome.	J Clin Exp Neuropsychol 1998 Apr;20(2):144-56	This study was designed to provide an estimate of the prevalence of neuropsychological impairment in chronic fatigue syndrome (CFS), to evaluate the concordance between impairment found on standardized tests and self-reported neuropsychological problems, and to study the relationship between neuropsychological functioning and fatigue severity and psychological processes. We adopted an individual approach to determine neuropsychological impairment as contrasted with the group-comparisons approach used in previous studies. Also, correction for premorbid functioning and confounders was done on an individual basis. The results show that a minority of participants were impaired in neuropsychological functioning. There was no relationship between neuropsychological impairment on standardized tests and self-reported memory and concentration problems. Neuropsychological functioning was not related to fatigue or depression. Slowed speed of information processing and motor speed were related to low levels of physical activity.
Vercoulen JH, Swanink CM, Galama JM, Fennis JF, Jongen PJ, Hommes OR, van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Hospital Nijmegen, The Netherlands.	The persistence of fatigue in chronic fatigue syndrome and multiple sclerosis: development of a model.	J Psychosom Res 1998 Dec;45(6):507-17	The cause of chronic fatigue syndrome (CFS) is unknown. With respect to factors perpetuating fatigue, on the other hand, a model has been postulated in the literature in which behavioral, cognitive, and affective factors play a role in perpetuating fatigue. In the present study, this hypothesized model was tested on patients with CFS and on fatigued patients with multiple sclerosis (MS). The model was formulated in terms of cause-and-effect relationships and an integral test of this model was performed by the statistical technique, "structural equation modeling," in 51 patients with chronic fatigue syndrome and 50 patients with multiple sclerosis matched for age, gender, and education. Attributing complaints to a somatic cause produced low levels of physical activity, which in turn had a causal effect on fatigue severity. Depression had to be deleted from the model. Sense of control over symptoms and focusing on bodily symptoms each

				had a direct causal effect on fatigue. The model showed an excellent fit for CFS patients, but was rejected for MS patients. Therefore, a new model for MS patients had to be developed in which sense of control had a causal effect on fatigue. In the MS model, no causal relationship was found between the physical state as measured by the Expanded Disability Status Score (EDSS) and fatigue or functional impairment. The present study shows that cognitive and behavioral factors are involved in the persistence of fatigue. Treatment should be directed at these factors. The processes involved in the subjective experience of fatigue in CFS were different from the processes related to fatigue in MS.
Vilikus Z, Mareckova H, Janatkova I, Krystufkova O, Barackova M, Boudova L, Brandejsky P, Fucikova T.	Ustav telovychovneho lekarstvi a Ustav klinicke imunologie 1. lekarske fakulty Univerzity Karlovy, Praha, Czech Republic. zdenek vilikus@medicom.cz	[Risk factors for ischemic heart disease in patients with chronic fatigue syndrome].[article in Czech]	Sb Lek 1998;99(1):53-61	Risk factors of coronary artery disease (CAD) between a group of patients suffering of chronic fatigue syndrome (CFS) and a control group of healthy persons (whose exercise activity was not health-limited) were compared. Thirty three patients (27 women, 6 men, average age 39.9 ± 11.7 years) and the same number of controls matched in age (39.8 ± 10.3 years), gender and body weight. The Minnesota Questionnaire (by Taylor) and the Compendium of Physical Activities (by Ainsworth) were used to estimate total energetic expenditure in exercise activity as well as in job. The risk factors of CAD in the patients with CFS were not higher than in the control group. Aerobic physical fitness, basic anthropometric data, blood pressure, spectrum of blood lipoproteins, blood uric acid and smoking habits were not different between the compared groups. Patients suffering from CFS had lower total energetic expenditure in exercise activity. Nevertheless, this significant difference in sports activity was not large enough to cause any difference in risk factors of CAD between the CFS patients and the control group.
Visser J, Blauw B, Hinloopen B, Brommer E, de Kloet ER, Kluft C, Nagelkerken L.	Division of Immunological and Infectious Diseases, TNO Prevention and Health, Leiden Amsterdam Center for Drug Research, The Netherlands.	CD4 T lymphocytes from patients with chronic fatigue syndrome have decreased interferon-gamma production and increased sensitivity to dexamethasone.	607: J Infect Dis 1998 Feb;177(2):451-4	A disturbed hypothalamus-pituitary-adrenal gland axis and alterations at the immune system level have been observed in patients with chronic fatigue syndrome (CFS). Glucocorticoids are known to modulate T cell responses; therefore, purified CD4 T cells from CFS patients were studied to determine whether they have an altered sensitivity to dexamethasone (DEX). CD4 T cells from CFS patients produced less interferon-gamma than did cells from controls; by contrast, interleukin-4 production and cell proliferation were comparable. With CD4 T cells from CFS patients (compared with cells from controls), a 10- to 20-fold lower DEX concentration was needed to achieve 50% inhibition of interleukin-4 production and proliferation, indicating an increased sensitivity to DEX in CFS patients. Surprisingly, interferon-gamma production in patients and controls was equally sensitive to DEX. A differential sensitivity of cytokines or CD4 T cell subsets to glucocorticoids might explain an altered immunologic function in CFS patients.
Vojdani A, Choppa PC, Tagle C, Andrin R, Samimi B, Lapp CW.	Immunosciences Laboratory, Beverly Hills, CA 90211, USA. immunsi@ix.netcom.com	Detection of Mycoplasma genus and Mycoplasma fermentans by PCR in patients with Chronic Fatigue Syndrome.	FEMS Immunol Med Microbiol 1998 Dec;22(4):355-65	Mycoplasma fermentans and other Mycoplasma species are colonizers of human mucosal surfaces and may be associated with human immunodeficiency virus infection. While many infectious agents have been described in different percentages of patients with Chronic Fatigue Syndrome (CFS), little is known about the prevalence of mycoplasmas and especially M. fermentans in CFS patients. A polymerase chain reaction (PCR)-based assay was used to detect Mycoplasma genus and M. fermentans genomes in peripheral blood mononuclear cells (PBMC) of CFS patients. Blood was collected from 100 patients with CFS and 50 control subjects. The amplified products of 717 bp of Mycoplasma genus, and 206 bp of M. fermentans were detected in DNA purified from blood samples in 52% and 34% of CFS samples, respectively. In contrast, these genomes were found in only 14% and 8% of healthy control subjects respectively (P < 0.0001). All samples were confirmed by Southern blot with a specific probe based on internal sequences of the expected amplification product. Several samples, which were positive for Mycoplasma genus, were negative for M. fermentans indicating that other Mycoplasma species are involved. A quantitative PCR was developed to determine the number of M. fermentans genome copies present in 1 microg of DNA for controls and CFS patients. Mycoplasma copy numbers ranging from 130 to 880 and from 264 to 2400 were detected in controls and CFS positive subjects, respectively. An enzyme immunoassay was applied for the detection of antibodies against p29 surface lipoprotein of M. fermentans to determine the relationship between M. fermentans genome copy numbers and antibody levels. Individuals with high genome copy numbers exhibited higher IgG and IgM antibodies against M. fermentans specific peptides. Isolation of this organism by culture from clinical specimens is needed in order to demonstrate specificity of signal detected by PCR in this study.
Vollmer-Conna U, Lloyd A, Hickie I, Wakefield D.	Inflammation Research Unit, School of Pathology, University of New South Wales, Sydney, Australia.	Chronic fatigue syndrome: an immunological perspective.	Aust N Z J Psychiatry 1998 Aug;32(4):523-7	OBJECTIVE: The aim of this study is to review research examining an immunological basis for chronic fatigue syndrome (CFS) and to discuss how a disturbance in immunity could produce central nervous system (CNS)-mediated symptoms. METHOD: Data relevant to the hypothesis that abnormal cytokine release plays a role in the pathogenesis of CFS are reviewed as well as recent evidence relating to potential

				mechanisms by which immune products may enter the brain and produce a disturbance in CNS processes. RESULTS: Examinations of cytokine levels in patients with CFS have produced inconclusive results. Recent evidence suggests that abnormal release of cytokines within the CNS may cause neural dysfunction by a variety of complex mechanisms. CONCLUSION: Neuropsychiatric symptoms in patients with CFS may be more closely related to disordered cytokine production by glial cells within the CNS than to circulating cytokines. This possibility is discussed in the context of unresolved issues in the pathogenesis of CFS. Review Literature
Ware NC.	Department of Social Medicine, Harvard Medical School, Boston, Massachusetts 02115, USA. nware@warren.med.harvard.edu	Sociosomatics and illness in chronic fatigue syndrome.	Psychosom Med 1998 Jul-Aug;60(4):394-401 Comment in: Psychosom Med. 1999 Mar-Apr;61(2):256	OBJECTIVE: This study examines social processes that construct the course of chronic illness. Specifically, it identifies and describes mechanisms that constitute the process of role constriction in employment for individuals with chronic illness. METHOD: Sixty-six persons meeting the Centers for Disease Control case definition of chronic fatigue syndrome (CFS) participated in a longitudinal study involving three waves of data collection over 3 years. Qualitative and quantitative methods were combined in the research, which included face-to-face semistructured interviews, telephone interviews, and self-report questionnaires. Materials presented in this study are drawn principally from the Year 1 face-to-face and telephone interviews. RESULTS: When patterns of symptoms and of the illness course in CFS intersect with work requirements, they impede performance and place ill individuals at risk for job loss. Persons with CFS devise and implement specific strategies to resist role constriction and remain in the work force. CONCLUSIONS: Role constriction is a social process of marginalization in chronic illness. Opposing forces of marginalization and resistance define the social course in chronic illness and suggest that chronicity can be thought of as a marginalized position in social space.
Watson WS, Donald C. McMillan, Abhijit Chaudhuri, Peter O. Behan		Increased Resting Energy Expenditure in the Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998; 4(4): 3 - 14	It has been suggested that resting energy expenditure may be raised in chronic fatigue syndrome due to an upregulation of transmembrane ion transport. We measured resting energy expenditure by indirect calorimetry in 11 women with chronic fatigue and in 11 healthy women. Total body potassium, by whole body counting, and total body water, extracellular water and intracellular water, by a bioelectrical impedance method, were also measured. When individual resting energy expenditure was predicted on the basis of total body potassium values for the chronic fatigue group, 5 out of 11 of these subjects had resting energy expenditure above the upper limit of normal as defined by the control group data. This is consistent with the hypothesis that there is upregulation of the sodium-potassium pump in chronic fatigue syndrome.
Wearden AJ, Morriss RK, Mullis R, Strickland PL, Pearson DJ, Appleby L, Campbell IT, Morris JA.	University of Manchester, Department of Psychiatry, Withington Hospital.	Randomised, double-blind, placebo-controlled treatment trial of fluoxetine and graded exercise for chronic fatigue syndrome. Erratum in: Br J Psychiatry 1998 Jul;173:89 Comment in: Br J Psychiatry. 1998 Jun;172:491-2 Br J Psychiatry. 1998 Oct;173:353 Br J	Br J Psychiatry 1998 Jun;172:485-90	BACKGROUND: The Joint Working Group of the Royal Colleges of Physicians, Psychiatrists and General Practitioners (1996) recommended graded exercise and antidepressants for patients with chronic fatigue syndrome. We assessed efficacy and acceptability of these treatments. METHOD: Six-month prospective randomised placebo and therapist contact time controlled trial with allocation to one of four treatment cells: exercise and 20 mg fluoxetine, exercise and placebo drug, appointments only and 20 mg fluoxetine, appointments and placebo drug. Drug treatment was double blind and patients were blind to assignment to exercise or appointments. RESULTS: Ninety-six (71%) of 136 patients completed the trial. Patients were more likely to drop out of exercise than non-exercise treatment ($P = 0.05$). In an intention to treat analysis, exercise resulted in fewer patients with case level fatigue than appointments only at 26 weeks (12 (18%) v. 4 (6%) respectively $P = 0.025$) and improvement in functional work capacity at 12 ($P = 0.005$) and 26 weeks ($P = 0.03$). Fluoxetine had a significant effect on depression at week 12 only ($P = 0.04$). Exercise significantly improved health perception ($P = 0.012$) and fatigue ($P = 0.028$) at 28 weeks. CONCLUSIONS: Graded exercise produced improvements in functional work capacity and fatigue, while fluoxetine improved depression only.
Weiss B.	Department of Environmental Medicine, University of Rochester Medical Center, NY 14642, USA.	Neurobehavioral properties of chemical sensitivity syndromes.	Neurotoxicology 1998 Apr;19(2):259-68	Chemical sensitivity syndromes refers to aggregations of symptoms marked by largely subjective neurobehavioral complaints and hypothesized links to immune system dysfunction. The entities reviewed here consist of the Multiple Chemical Sensitivity Syndrome, the Sick Building Syndrome, the Chronic Fatigue Syndrome, and the Gulf War Syndrome. Except for the Chronic Fatigue Syndrome, toxic chemical exposures are accorded a significant role in their etiology. The connections are ambiguous because of the variety of chemical agents cited and, for the most part, the relatively low levels at which exposures occur. Conventional clinical signs are also typically lacking. Explanatory mechanisms include psychiatric diagnoses such as somatization, behavioral mechanisms such as conditioning and generalization, neuropharmacological mechanisms such as sensitization, and psychoneuroimmunological mechanisms such as those involving the hypothalamic-pituitary-adrenal axis. Laboratory animal experimentation and

				controlled clinical trials, especially with inhaled material, provide the means for exploring the proffered explanations.
Wessely S.		The epidemiology of chronic fatigue syndrome.	Epidemiol Psychiatr Soc 1998 Jan-Apr;7(1):10-24	
White PD, Thomas JM, Amess J, Crawford DH, Grover SA, Kangro HO, Clare AW.	St Bartholomew's, London.	Incidence, risk and prognosis of acute and chronic fatigue syndromes and psychiatric disorders after glandular fever.	Br J Psychiatry 1998 Dec;173:475-81	BACKGROUND: The role of viruses in the aetiology of both chronic fatigue syndrome (CFS) and depressive illness is uncertain. METHOD: A prospective cohort study of 250 primary care patients, presenting with glandular fever or an ordinary upper respiratory tract infection (URTI). RESULTS: The incidence of an acute fatigue syndrome was 47% at onset, after glandular fever, compared with 20% with an ordinary URTI (relative risk 2.3, 95% CI 1.3-4.1). The acute fatigue syndrome lasted a median (interquartile range) of eight weeks (4-16) after glandular fever, but only three weeks (2-4) after an URTI. The prevalence of CFS was 9-22% six months after glandular fever, compared with 0-6% following an ordinary URTI, with relative risks of 2.7-5.1. The most conservative measure of the incidence of CFS was 9% after glandular fever, compared with no cases after an URTI. A conservative estimate is that glandular fever accounts for 3113 (95% CI 1698-4528) new cases of CFS per annum in England and Wales. New episodes of major depressive disorder were triggered by infection, especially the Epstein-Barr virus, but lasted a median of only three weeks. No psychiatric disorder was significantly more prevalent six months after onset than before. CONCLUSIONS: Glandular fever is a significant risk factor for both acute and chronic fatigue syndromes. Transient new major depressive disorders occur close to onset, but are not related to any particular infection if they last more than a month.
Whiteside TL, Friberg D.	University of Pittsburgh Cancer Institute, Pennsylvania 15213-2582, USA.	Natural killer cells and natural killer cell activity in chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):27S-34S	Chronic fatigue syndrome (CFS) is associated with insidious and persistent immunologic abnormalities that have proved difficult to reproduce. The heterogeneity of CFS, the variable quality of immunologic assays and their performance, along with an almost complete absence of longitudinal studies of cellular immune abnormalities in CFS may explain this difficulty. However, in a significant proportion of cases, low levels of natural killer (NK) cell activity have been reported. This article will explore the mechanisms responsible for low NK cell activity, discuss the relation between levels of NK cell activity and health/disease, describe new findings on NK cell-brain interactions, and put forth a specific hypothesis for the role of NK cells in the pathogenesis of CFS.
Wilke WS, Fouad-Tarazi FM, Cash JM, Calabrese LH.	Department of Rheumatic and Immunologic Disease, Cleveland Clinic Foundation, OH 44195, USA.	The connection between chronic fatigue syndrome and neurally mediated hypotension.	Cleve Clin J Med 1998 May;65(5):261-6	Research from several groups of investigators indicates that some patients with chronic fatigue syndrome have abnormal vasovagal or vasodepressor responses to upright posture. If confirmed, these findings may explain some of the symptoms of chronic fatigue syndrome. There is also speculation that neurally mediated hypotension may be present in fibromyalgia. This article discusses the original research in this area, the results of follow-up studies, and the current approach to treating patients with chronic fatigue syndrome in whom neurally mediated hypotension is suspected.
Wood B, Wessely S, Papadopoulos A, Poon L, Checkley S.	Institute of Psychiatry, London, UK.	Salivary cortisol profiles in chronic fatigue syndrome.	Neuropsychobiology 1998;37(1):1-4	Salivary cortisol profiles (hourly sampling over a 16-hour period) of 10 patients with chronic fatigue syndrome (CFS) but without concurrent depressive disorder were compared with those of 10 healthy volunteers matched for age, sex and menstrual cycle. The mean saliva cortisol concentration over the 16-hour period was slightly but significantly greater in the patients than the controls ($p < 0.05$). These findings are at variance with earlier reports that CFS is a hypocortisolaemic state and suggest that in CFS the symptom of fatigue is not caused by hypocortisolaemia.
Wright JB, Beverley DW.	Lime Trees Child and Family Unit, York, UK.	Chronic fatigue syndrome.	Arch Dis Child 1998 Oct;79(4):368-74	
Young AH, Sharpe M, Clements A, Dowling B, Hawton KE, Cowen PJ.	University Department of Psychiatry, Warneford Hospital, Oxford, United Kingdom.	Basal activity of the hypothalamic-pituitary-adrenal axis in patients with the chronic fatigue syndrome (neurasthenia).	Biol Psychiatry 1998 Feb 1;43(3):236-7	BACKGROUND: Impairments in both basal activity and activation of the hypothalamic-pituitary-adrenal axis (HPA) have been reported in chronic fatigue syndrome (CFS; neurasthenia). We sought to replicate these findings and examined basal activity of the HPA in a carefully selected sample of patients with CFS. METHODS: Basal activity of the HPA was assessed using salivary and urinary cortisol collection over a 24-hour period in 22 (12 male; 10 female) patients meeting criteria for CFS and appropriate controls. RESULTS: Salivary and urinary cortisol measures did not differ between CFS patients and controls. CONCLUSIONS: Basal activity of the HPA was not reduced in CFS patients. Reasons for the failure to replicate previous findings are discussed.